

L2

chain nodes :

21 22 23

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

chain bonds :

4-23 16-21 21-22 22-23

ring bonds :

1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13 13-14 15-16 15-20  
16-17 17-18 18-19 19-20

exact/norm bonds :

1-2 1-6 3-4 4-5 4-23 15-16 15-20 16-17 16-21 17-18 18-19 19-20

exact bonds :

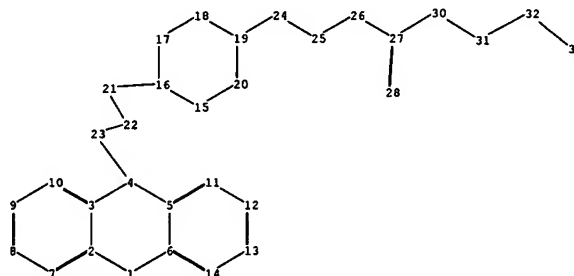
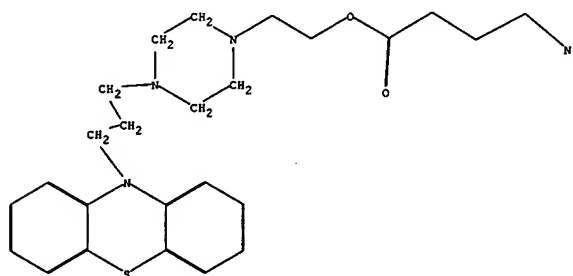
21-22 22-23

normalized bonds :

2-3 2-7 3-10 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13 13-14

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom  
13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS22:CLASS23:CLASS



L12

chain nodes :

21 22 23 24 25 26 27 28 30 31 32 33

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

chain bonds :

4-23 16-21 19-24 21-22 22-23 24-25 25-26 26-27 27-28 27-30 30-31 31-32 32-33

ring bonds :

1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13 13-14 15-16 15-20  
16-17 17-18 18-19 19-20

exact/norm bonds :

1-2 1-6 3-4 4-5 19-24 25-26 26-27 27-28 32-33

exact bonds :

4-23 15-16 15-20 16-17 16-21 17-18 18-19 19-20 21-22 22-23 24-25 27-30 30-31 31-32

normalized bonds :

2-3 2-7 3-10 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13 13-14

isolated ring systems :

containing 1 : 15 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom  
13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS  
24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS

10/808,541

=> d his

(FILE 'HOME' ENTERED AT 09:47:13 ON 12 JUL 2006)

FILE 'REGISTRY' ENTERED AT 09:47:19 ON 12 JUL 2006  
ACTIVATEA10808541/Q A10808541/Q

L1 STR  
-----  
ACTIVATE B10808541/A  
-----  
L2 STR  
L3 ( 3474)SEA FILE=REGISTRY SSS FUL L2  
L4 STR  
L5 498 SEA FILE=REGISTRY SUB=L3 SSS FUL L4  
-----  
L6 STRUCTURE UPLOADED  
L7 375 S L6 SUB=L5 FUL  
L8 123 S L5 NOT L7

FILE 'CAPLUS' ENTERED AT 09:50:39 ON 12 JUL 2006  
L9 650 S L7  
L10 ANALYZE L9 1- RN HIT : 238 TERMS

FILE 'REGISTRY' ENTERED AT 09:51:45 ON 12 JUL 2006  
L11 6 S 5002-47-1/RN OR 84-06-0/RN OR 2746-81-8/RN OR 388-51-2/RN OR  
L12 STRUCTURE UPLOADED  
L13 10 S L12 SUB=L5 FUL

FILE 'CAPLUS' ENTERED AT 09:54:31 ON 12 JUL 2006  
L14 5 S L13

FILE 'CAPLUS' ENTERED AT 09:54:46 ON 12 JUL 2006  
L15 1 S US20040242570/PN  
SELECT RN L15 1-

FILE 'REGISTRY' ENTERED AT 09:55:19 ON 12 JUL 2006  
L16 69 S E1-69  
L17 18 S 6-6-6/SZ AND L16  
L18 51 S L16 NOT L17  
L19 11 S L18 AND NRS=1  
L20 24 S L18 AND NRS>1  
L21 16 S L18 NOT (L19 OR L20)

FILE 'CAPLUS' ENTERED AT 10:03:31 ON 12 JUL 2006

FILE 'REGISTRY' ENTERED AT 10:03:43 ON 12 JUL 2006  
L22 17 S L17 NOT C12 H9 N S/MF

FILE 'CAPLUS' ENTERED AT 10:04:37 ON 12 JUL 2006  
L23 15730 S L22

FILE 'REGISTRY' ENTERED AT 10:05:04 ON 12 JUL 2006  
L24 1 S PIPERAZINE/CN  
L25 691215 S 46.383.1/RID  
L26 15 S L17 AND L25  
L27 1 S L17 NOT L22  
L28 34120 S C4NS-C6-C6/EA

10/808,541

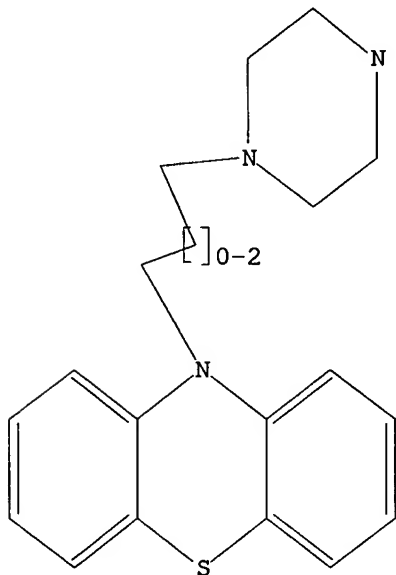
L29 14 S L26 AND L28

FILE 'CAPLUS' ENTERED AT 10:06:33 ON 12 JUL 2006  
L30 3111 S L29  
L31 ANALYZE L30 1- RN HIT : 14 TERMS

FILE 'REGISTRY' ENTERED AT 10:09:59 ON 12 JUL 2006  
L32 3 S 69-23-8/RN OR 58-39-9/RN OR 84-06-0/RN  
L33 11 S L29 NOT L32

FILE 'CAPLUS' ENTERED AT 10:10:39 ON 12 JUL 2006  
L34 1 S L33  
L35 1 S L32 AND L34  
L36 5 S L14 OR L35

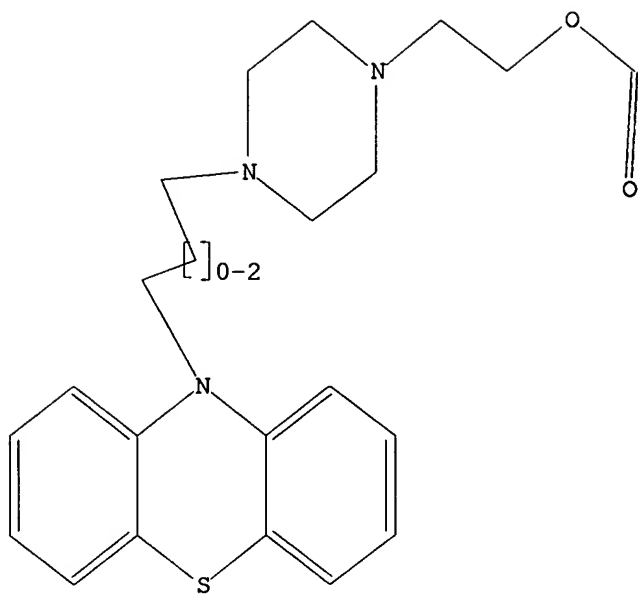
=> d 12  
L2 HAS NO ANSWERS  
L2 STR



Structure attributes must be viewed using STN Express query preparation.

=> d 14  
L4 HAS NO ANSWERS  
L4 STR

10/808,541



Structure attributes must be viewed using STN Express query preparation.

=> d ibib abs hitstr total

10/808,541

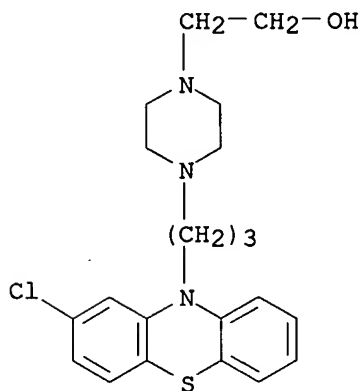
L36 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:261599 CAPLUS  
 DOCUMENT NUMBER: 138:265698  
 TITLE: Organic acid-conjugated antipsychotic drugs, and  
 therapeutic use thereof  
 INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada; Gil-Ad, Irit;  
 Weizman, Abraham  
 PATENT ASSIGNEE(S): Ramot at Tel Aviv University Ltd., Israel; Bar Ilan  
 University  
 SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026563	A2	20030403	WO 2002-IL795	20020929
WO 2003026563	A3	20040318		
WO 2003026563	C2	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2461663	AA	20030403	CA 2002-2461663	20020929
EP 1429844	A2	20040623	EP 2002-772790	20020929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005503423	T2	20050203	JP 2003-530202	20020929
CN 1596141	A	20050316	CN 2002-823600	20020929
AU 2004201240	A1	20040506	AU 2004-201240	20040325
US 2004242570	A1	20041202	US 2004-808541	20040325
WO 2005092392	A2	20051006	WO 2005-IL341	20050327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2001-324936P	P 20010927
			WO 2002-IL795	W 20020929
			US 2004-808541	A 20040325

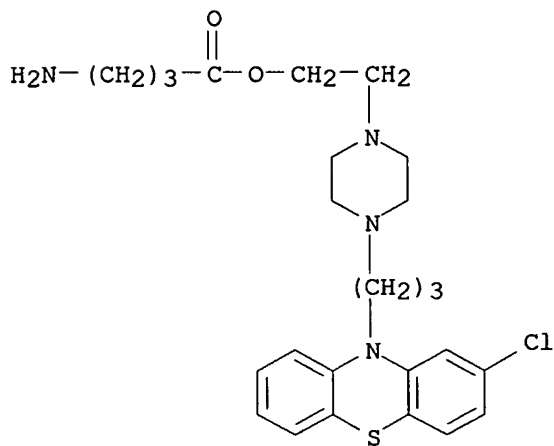
AB Chemical conjugates of anti-psychotic drugs and organic acids, uses thereof in  
 the treatment of psychotic and/or proliferative disorders and diseases and  
 as chemosensitizing agents, and their syntheses, are disclosed. The organic  
 acids are selected to reduce side effects induced by the anti-psychotic

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- drugs and/or to exert an anti-proliferative activity.
- IT 58-39-9, Perphenazine  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
(organic acid-conjugated antipsychotic drugs, and therapeutic use)
- RN 58-39-9 CAPLUS
- CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]- (9CI)  
(CA INDEX NAME)



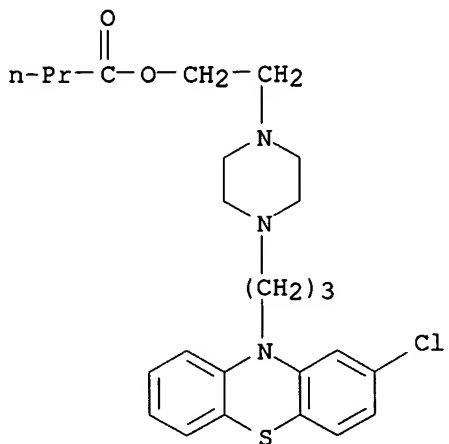
- IT 503537-33-5P 503569-71-9P, AN 167  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(organic acid-conjugated antipsychotic drugs, and therapeutic use)
- RN 503537-33-5 CAPLUS
- CN Butanoic acid, 4-amino-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 503569-71-9 CAPLUS

CN Butanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

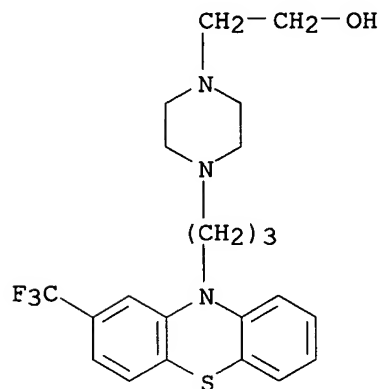


IT 69-23-8, Fluphenazine

RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
(organic acid-conjugated antipsychotic drugs, and therapeutic use)

RN 69-23-8 CAPLUS

CN 1-Piperazineethanol, 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]- (9CI) (CA INDEX NAME)



IT 1063-36-1P, AN 181 503569-70-8P, AN 130  
503569-72-0P, AN 177 503569-73-1P 503569-74-2P  
, AN 179 503569-75-3P, AN 187

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(organic acid-conjugated antipsychotic drugs, and therapeutic use)

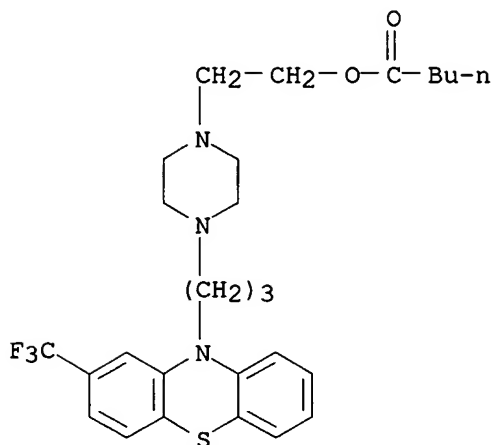
RN 1063-36-1 CAPLUS

CN Pentanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-



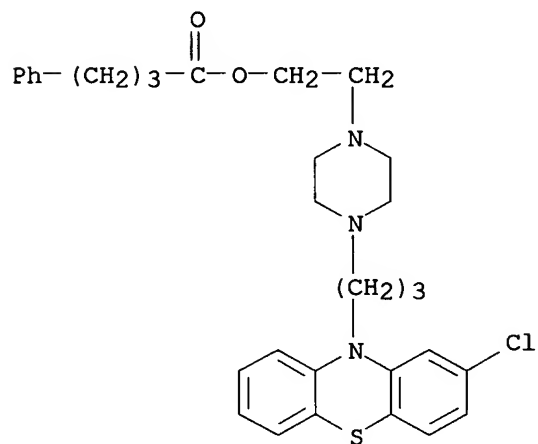
10/808,541

yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



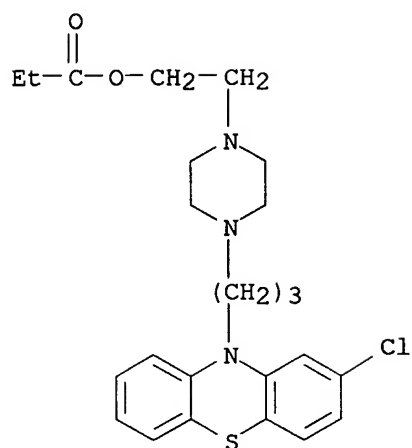
RN 503569-70-8 CAPLUS

CN Benzenebutanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



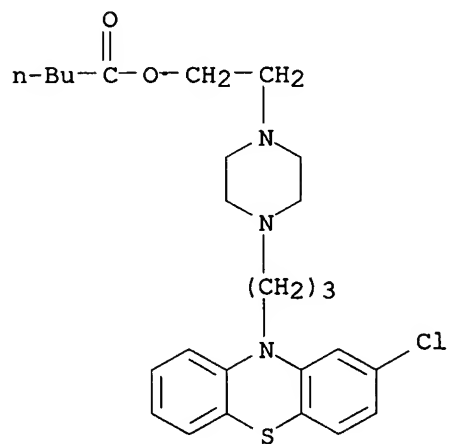
RN 503569-72-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, propanoate (ester) (9CI) (CA INDEX NAME)



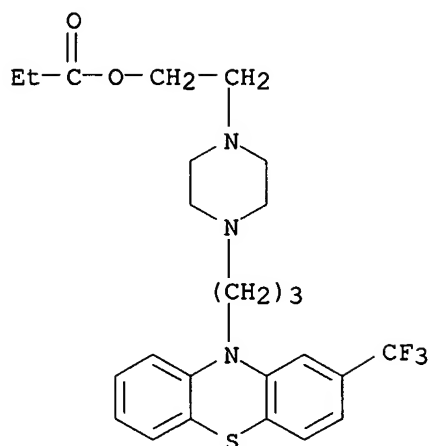
RN 503569-73-1 CAPLUS

CN Pentanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



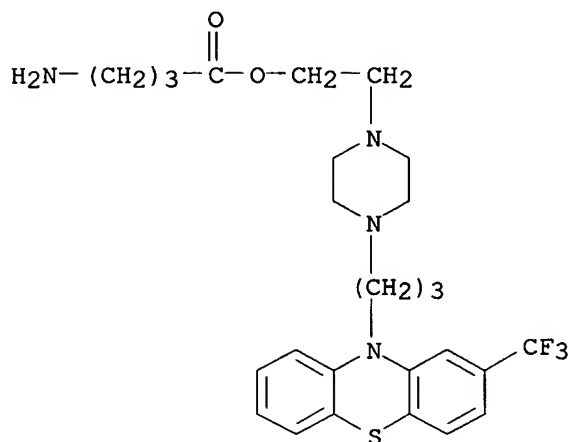
RN 503569-74-2 CAPLUS

CN 1-Piperazineethanol, 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-, propanoate (ester) (9CI) (CA INDEX NAME)



RN 503569-75-3 CAPLUS

CN Butanoic acid, 4-amino-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

IT 58-39-9D, Perphenazine, organic acid conjugates 69-23-8D, Fluphenazine, organic acid conjugates 84-06-0D, Thiopropazate, organic acid conjugates

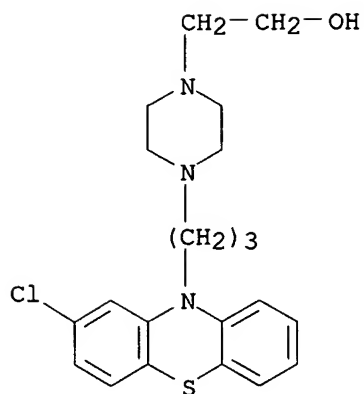
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(organic acid-conjugated antipsychotic drugs, and therapeutic use)

RN 58-39-9 CAPLUS

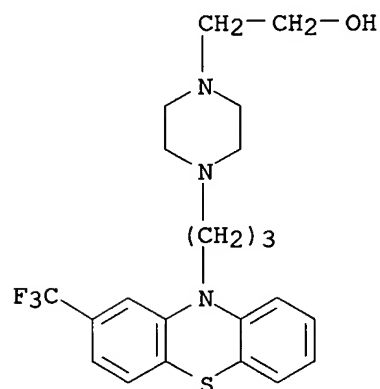
CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]- (9CI) (CA INDEX NAME)

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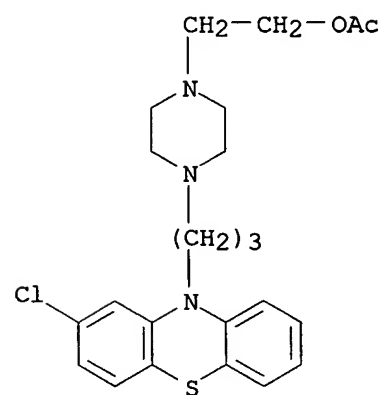
RN 69-23-8 CAPLUS

CN 1-Piperazineethanol, 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]- (9CI) (CA INDEX NAME)

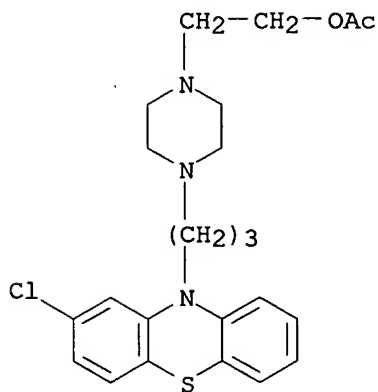


RN 84-06-0 CAPLUS

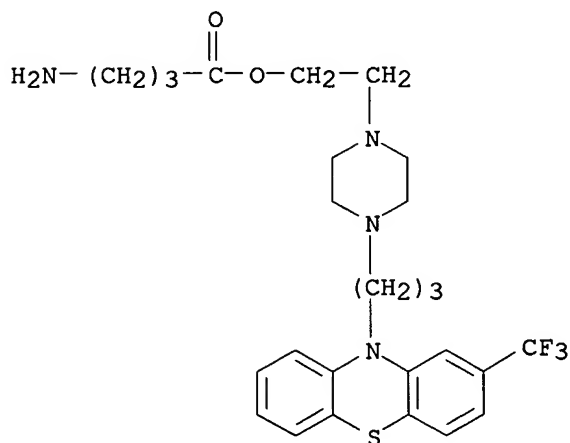
CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)



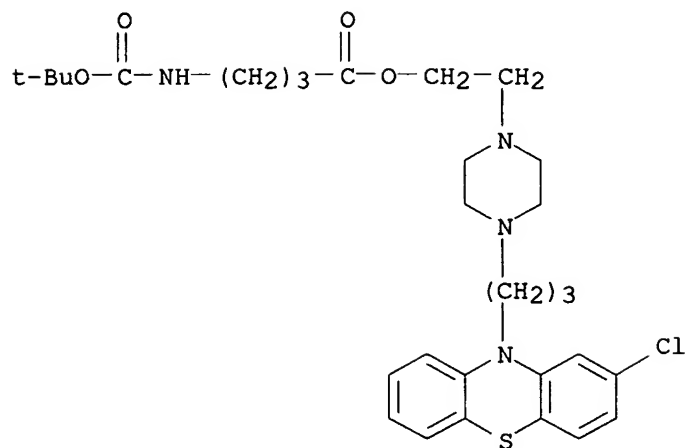
IT 84-06-0, Thiopropazate 503537-31-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (organic acid-conjugated antipsychotic drugs, and therapeutic use)  
 RN 84-06-0 CAPLUS  
 CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)



RN 503537-31-3 CAPLUS  
 CN Butanoic acid, 4-amino-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

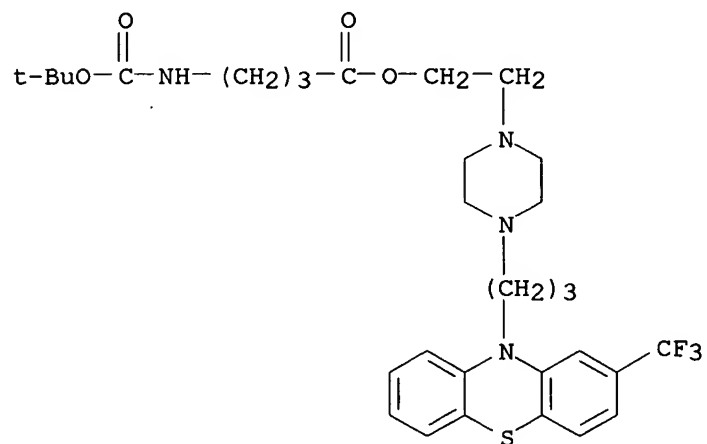


IT 503537-30-2P 503537-32-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (organic acid-conjugated antipsychotic drugs, and therapeutic use)  
 RN 503537-30-2 CAPLUS  
 CN Butanoic acid, 4-[[[1,1-dimethylethoxy)carbonyl]amino]-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 503537-32-4 CAPLUS

CN Butanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]-,  
2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-  
piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L36 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:132193 CAPLUS

DOCUMENT NUMBER: 98:132193

TITLE: Prolongation of the action of intramuscular formulations of phenothiazines

AUTHOR(S): Florence, A. T.; Vezin, W. R.

CORPORATE SOURCE: Dep. Pharm., Univ. Strathclyde, Glasgow, G1 1XW, UK

SOURCE: Alfred Benzon Symposium (1982), Volume Date 1981, 17(Optim. Drug Delivery), 93-113  
CODEN: ABSYB2; ISSN: 0105-3639

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A number of phenothiazine esters were examined for their ability to prolong drug action on i.m. administration. The rank order of embonate esters was fluphenazine > trifluoperazine > pericyazine and may be related to solubility of the salts, the least soluble being longest acting. For liposol. esters, changing the oil phase or lipophilicity was studied. Decreasing activity of drug with increasing ester chain length was shown for C10, C16, and C18 esters of fluphenazine. Also formulation of the esters in suspensions increased activity compared to solns. in oils except when particle size was increased >20  $\mu$ m. Microencapsulation with polymers did not show much promise. Fluphenazine esters were also embedded in solid particles of poly(alkyl cyanoacrylates). Promising results were shown for fluphenazine diesters with azaleic and dodecanedicarboxylic acids. Polymerized forms of the drug were disappointing in terms of extended duration of activity but provided some useful data on the parameters affecting biodegradability and activity of the polymers.

IT 73310-61-9

RL: BIOL (Biological study)

(prolonged-action i.m. formulation in relation to)

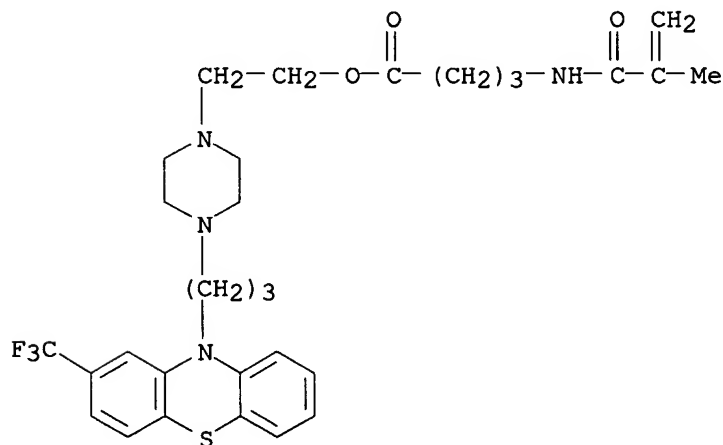
RN 73310-61-9 CAPLUS

CN Butanoic acid, 4-[(2-methyl-1-oxo-2-propenyl)amino]-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, homopolymer (9CI) (CA INDEX NAME)

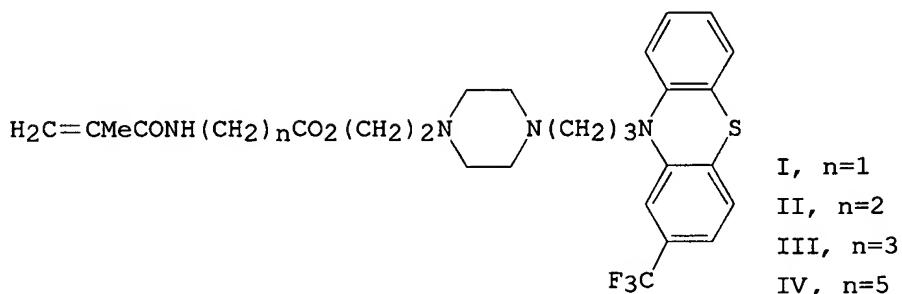
CM 1

CRN 73310-60-8

CMF C30 H37 F3 N4 O3 S



L36 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1980:153009 CAPLUS  
 DOCUMENT NUMBER: 92:153009  
 TITLE: Biologically active poly(N-methacryloyl ω-amino acid) esters of fluphenazine and their duration of activity  
 AUTHOR(S): Vezin, W. R.; Florence, A. T.  
 CORPORATE SOURCE: Dep. Pharm., Univ. Strathclyde, Glasgow, G1 1XW, UK  
 SOURCE: Journal of Pharmacy and Pharmacology (1979), 31, Suppl.(Br. Pharm. Conf. 1979), 63P  
 CODEN: JPPMAB; ISSN: 0022-3573  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB Homopolymers of the fluphenazine esters I-IV, and copolymers of these esters with hydrophilic methacrylates were prepared and their biol. activity tested in a rat conditioning test. Of the homopolymers, those with monomers I and IV were inactive while those with monomers II and III were active; this correlated with their biodegradability. Degradability and hence activity increased with decreasing particle size, but were not enhanced by copolymn. with .apprx.20% methacrylic acid.

IT 73310-61-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prodrug, preparation and biol. activity of)

RN 73310-61-9 CAPLUS

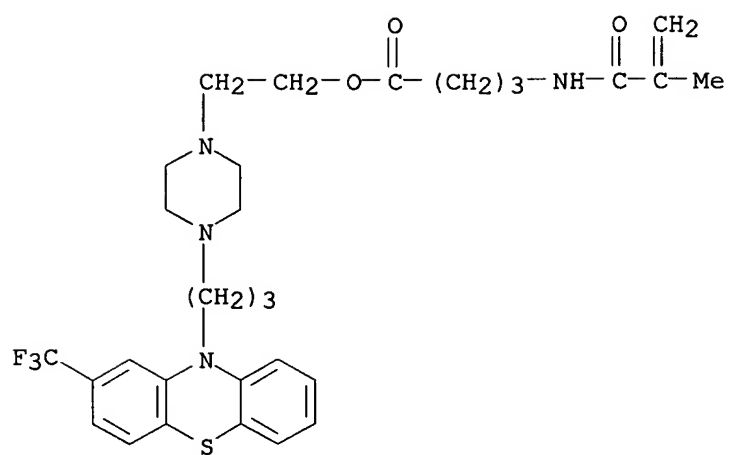
CN Butanoic acid, 4-[(2-methyl-1-oxo-2-propenyl)amino]-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 73310-60-8

CMF C30 H37 F3 N4 O3 S





L36 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1979:588466 CAPLUS

DOCUMENT NUMBER: 91:188466

TITLE: Affinity chromatography: new resins for the isolation of glutamate dehydrogenase and study of its structure and binding of drugs

AUTHOR(S): Veronese, F. M.; Schiavon, O.; Boccu, E.; Largajolli, R.; Benassi, C. A.

CORPORATE SOURCE: Ist. Chim. Farm., Univ. Padova, Padua, Italy

SOURCE: Farmaco, Edizione Pratica (1979), 34(6), 266-76

CODEN: FRPPAO; ISSN: 0430-0912

DOCUMENT TYPE: Journal

LANGUAGE: Italian

AB Procedures are given for preparing 7 affinity chromatog. resins for glutamate dehydrogenase, using various inhibitors, substrates, and psychotropic phenothiazines (which are also inhibitors of the enzyme) as ligands. The preps. were: (1) aminoisophthalic acid linked to epoxy-activated Sepharose 6B; (2) aminoisophthalic acid linked to CNBr-activated Sepharose 4B; (3) glutamic acid linked to epoxy-activated Sepharose 6B; (4) Dextran Blue linked to CNBr-activated Sepharose 4B; (5) didemethylchlorpromazine linked to CNBr-activated Sepharose 4B; (6)  $\omega$ -O-succinylperfenazine linked to carbodiimide-activated aminohexamethylene-Sepharose 4B; and (7) perfenazine linked to epoxy-activated Sepharose 6B. The 1st 4 preps. were evaluated for use in isolation and structural studies of the enzyme and the last 3 for use in studying its drug-binding properties. Preps. 1 and 4 could be used to isolate the enzyme from tuna liver (which was eluted in high yield by buffers containing NAD or ADP), but not the enzyme from beef liver. Preps. 6 and 7 possessed properties suitable for the study of drug-glutamic dehydrogenase binding. The way in which the ligand was attached to the resin matrix markedly affected its enzyme-binding properties.

IT 70213-24-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and glutamate dehydrogenase affinity chromatog. on)

RN 70213-24-0 CAPLUS

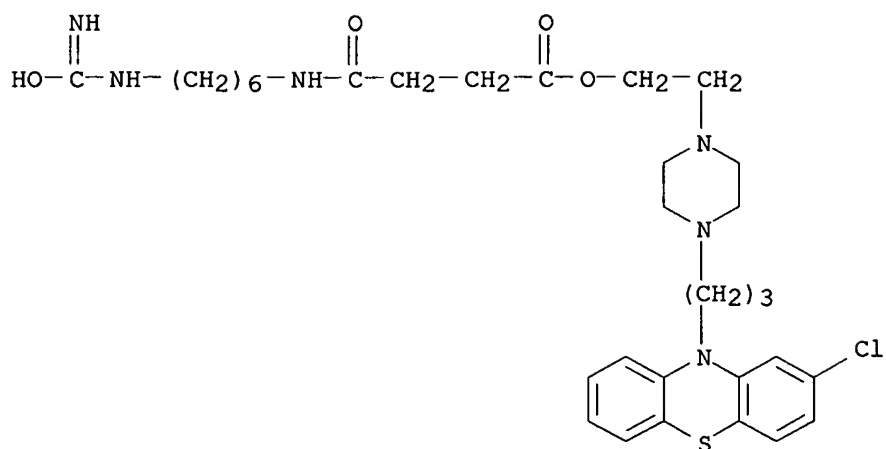
CN Agarose, [6-[[4-[2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethoxy]-1,4-dioxobutyl]amino]hexyl]carbamimidate (9CI) (CA INDEX NAME)

CM 1

CRN 173243-99-7

CMF C32 H45 Cl N6 O4 S

10/808,541



CM 2

CRN 9012-36-6

CMF Unspecified

CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L36 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1979:179887 CAPLUS

DOCUMENT NUMBER: 90:179887

TITLE: Drug-protein interactions: evaluation of the binding of antipsychotic drugs to glutamate dehydrogenase by quantitative affinity chromatography

AUTHOR(S): Veronese, F. M.; Bevilacqua, R.; Chaiken, I. M.

CORPORATE SOURCE: Inst. Pharm. Chem., Univ. Padova, Padua, Italy

SOURCE: Molecular Pharmacology (1979), 15(2), 313-21

CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interactions of psychoactive drugs with bovine glutamate dehydrogenase [9029-12-3] were evaluated by quant. affinity chromatog. on Perphenazine-Sepharose. An affinity matrix containing a relatively low d. of immobilized ligand was used to achieve competitive elution of zones of the enzyme with buffers containing soluble phenothiazines and butyrophenones.

These

competitive elution data indicated that all of the drugs tested bind at the same protein site. The variation of elution volume with soluble drug concentration allowed the calcn. of apparent dissociation consts. for the

binding of

these substances. Especially among the phenothiazines, the relative magnitudes of the dissociation consts. for the various drugs were similar both to the relative inhibitory effects by these substances on dehydrogenase catalysis and to their relative pharmacol. potencies. A close but nondirect interrelation between drug, NADH, and GTP binding to glutamate dehydrogenase was observed by chromatog. elutions with various combinations of these substances in the eluting buffers.

IT 70213-24-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 70213-24-0 CAPLUS

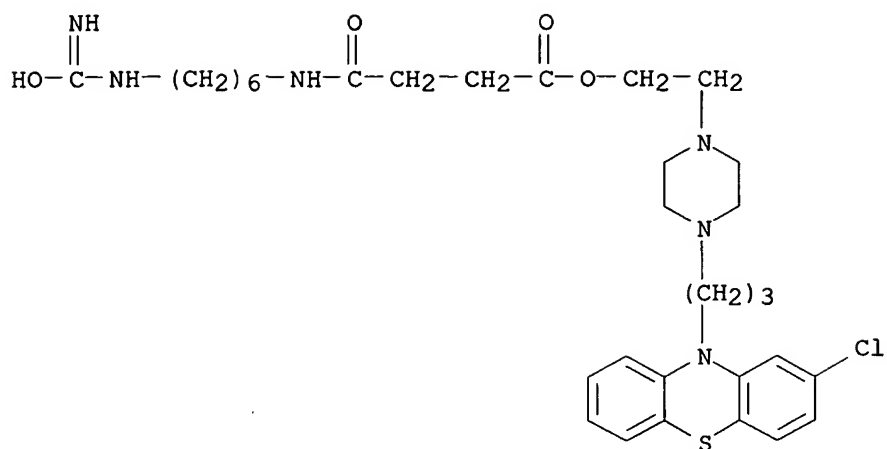
CN Agarose, [6-[[4-[2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethoxy]-1,4-dioxobutyl]amino]hexyl]carbamide (9CI) (CA INDEX NAME)

CM 1

CRN 173243-99-7

CMF C32 H45 C1 N6 O4 S

10/808,541



CM 2

CRN 9012-36-6

CMF Unspecified

CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

10/808,541

=> => d his

(FILE 'HOME' ENTERED AT 09:47:13 ON 12 JUL 2006)

FILE 'REGISTRY' ENTERED AT 09:47:19 ON 12 JUL 2006  
ACTIVATEA10808541/Q A10808541/Q

L1 STR  
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ACTIVATE B10808541/A  
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L2 STR  
L3 ( 3474)SEA FILE=REGISTRY SSS FUL L2  
L4 STR  
L5 498 SEA FILE=REGISTRY SUB=L3 SSS FUL L4  
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L6 STRUCTURE UPLOADED  
L7 375 S L6 SUB=L5 FUL  
L8 123 S L5 NOT L7

FILE 'CAPLUS' ENTERED AT 09:50:39 ON 12 JUL 2006  
L9 650 S L7  
L10 ANALYZE L9 1- RN HIT : 238 TERMS

FILE 'REGISTRY' ENTERED AT 09:51:45 ON 12 JUL 2006  
L11 6 S 5002-47-1/RN OR 84-06-0/RN OR 2746-81-8/RN OR 388-51-2/RN OR  
L12 STRUCTURE UPLOADED  
L13 10 S L12 SUB=L5 FUL

FILE 'CAPLUS' ENTERED AT 09:54:31 ON 12 JUL 2006  
L14 5 S L13

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L15 1 S US20040242570/PN  
SELECT RN L15 1-

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L16 69 S E1-69  
L17 18 S 6-6-6/SZ AND L16  
L18 51 S L16 NOT L17  
L19 11 S L18 AND NRS=1  
L20 24 S L18 AND NRS>1  
L21 16 S L18 NOT (L19 OR L20)

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FILE 'REGISTRY' ENTERED AT 10:03:43 ON 12 JUL 2006  
L22 17 S L17 NOT C12 H9 N S/MF

FILE 'CAPLUS' ENTERED AT 10:04:37 ON 12 JUL 2006  
L23 15730 S L22

FILE 'REGISTRY' ENTERED AT 10:05:04 ON 12 JUL 2006  
L24 1 S PIPERAZINE/CN  
L25 691215 S 46.383.1/RID  
L26 15 S L17 AND L25  
L27 1 S L17 NOT L22  
L28 34120 S C4NS-C6-C6/EA

10/808,541

L29            14 S L26 AND L28

FILE 'CAPLUS' ENTERED AT 10:06:33 ON 12 JUL 2006

L30           3111 S L29

L31           ANALYZE L30 1- RN HIT :        14 TERMS

FILE 'REGISTRY' ENTERED AT 10:09:59 ON 12 JUL 2006

L32           3 S 69-23-8/RN OR 58-39-9/RN OR 84-06-0/RN

L33           11 S L29 NOT L32

FILE 'CAPLUS' ENTERED AT 10:10:39 ON 12 JUL 2006

L34           1 S L33

L35           1 S L32 AND L34

L36           5 S L14 OR L35

L37           21 S L9 AND ADV/RL

L38           29 S L9 AND PAC/RL

L39           339 S L9 AND BIOL/RL

L40           42 S L37 OR L38

L41           42 S L39 AND L40

=> d ibib abs hitstr total

L41 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:493804 CAPLUS

DOCUMENT NUMBER: 144:481058

TITLE: Methods and pharmaceutical compositions using fluphenazine ester derivatives for modulating high-density lipoprotein cholesterol levels

INVENTOR(S): Friedman, Jonathan M.

PATENT ASSIGNEE(S): Fazix Corporation., USA

SOURCE: U.S. Pat. Appl. Publ., 17 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111346	A1	20060525	US 2005-286220	20051123
WO 2006058199	A1	20060601	WO 2005-US42721	20051123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:

US 2004-630293P P 20041123

AB The invention discloses a method for modulating high-d. lipoprotein cholesterol levels in a mammal by administering to the mammal a therapeutically effective amount of a fluphenazine ester derivative. Pharmaceutical formulations for administration of the fluphenazine ester derivative are also disclosed. Results with fluphenazine 4-chlorophenoxyisobutyric acid ester (prepared by a referenced protocol and identity confirmed) are presented.

IT 76674-41-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

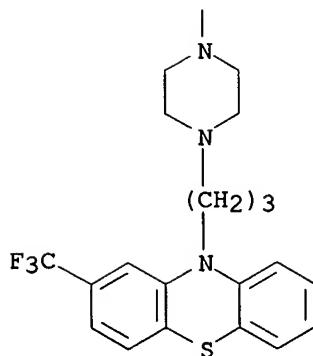
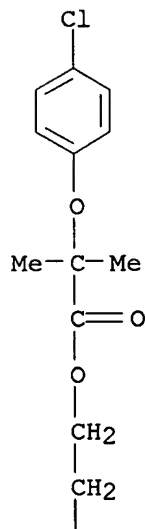
(Preparation); USES (Uses)

(fluphenazine ester derivs. for modulating HDL cholesterol levels)

RN 76674-41-4 CAPLUS

CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





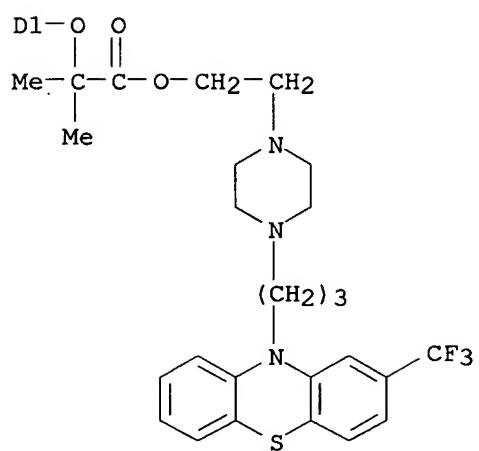
IT 887259-67-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(fluphenazine ester derivs. for modulating HDL cholesterol levels)  
RN 887259-67-8 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A



D1-C1

PAGE 2-A



141 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:99736 CAPLUS

DOCUMENT NUMBER: 144:184692

TITLE: Use of compounds active on the sigma receptor for the treatment of mechanical allodynia

INVENTOR(S): Baeyens Cabrera, Jose Manuel

PATENT ASSIGNEE(S): Laboratorios Del Dr. Esteve, S.A., Spain

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010587	A1	20060202	WO 2005-EP8080	20050725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006019968	A1	20060126	US 2004-902272	20040730
US 2006019969	A1	20060126	US 2004-902273	20040730
PRIORITY APPLN. INFO.:			EP 2004-17561	A 20040724
			EP 2004-17562	A 20040724
			US 2004-902272	A 20040730
			US 2004-902273	A 20040730
			EP 2004-20376	A 20040827

OTHER SOURCE(S): MARPAT 144:184692

AB The invention discloses the use of compds. active on the sigma receptor for the treatment of mech. allodynia.

IT 2376-65-0 3105-68-8 874882-85-6

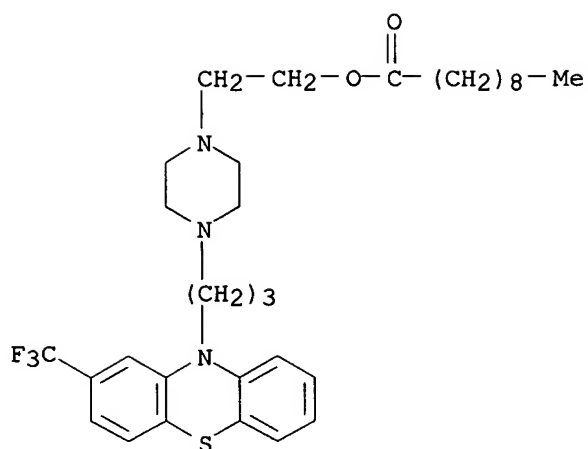
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(sigma receptor modulators for treatment of mech. allodynia)

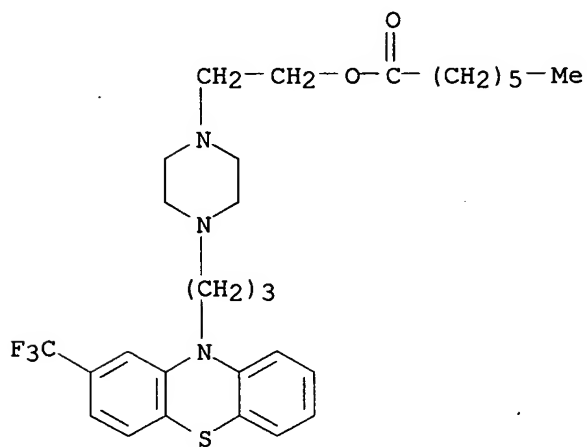
RN 2376-65-0 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

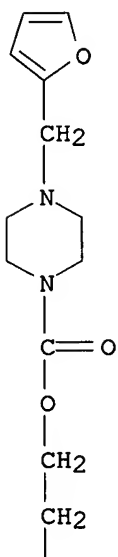
RN 3105-68-8 CAPLUS  
 CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



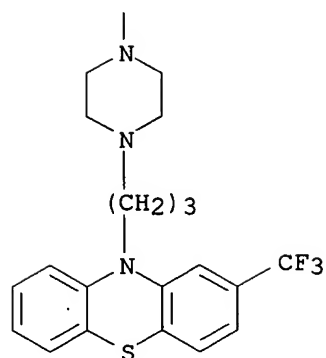
●2 HCl

RN 874882-85-6 CAPLUS  
 CN 1-Piperazinecarboxylic acid, 4-(2-furanylmethyl)-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/808,541

ANSWER 3 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2006:13077 CAPLUS  
DOCUMENT NUMBER: 144:64395  
TITLE: Intralesional treatment of psoriasis  
INVENTOR(S): Roth, Stephen; More, Robert; Jameson, Bradford A.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S.  
Ser. No. 13,969.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006003996	A1	20060105	US 2005-155450	20050617
WO 2003106660	A2	20031224	WO 2003-US19595	20030617
WO 2003106660	A3	20040617		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

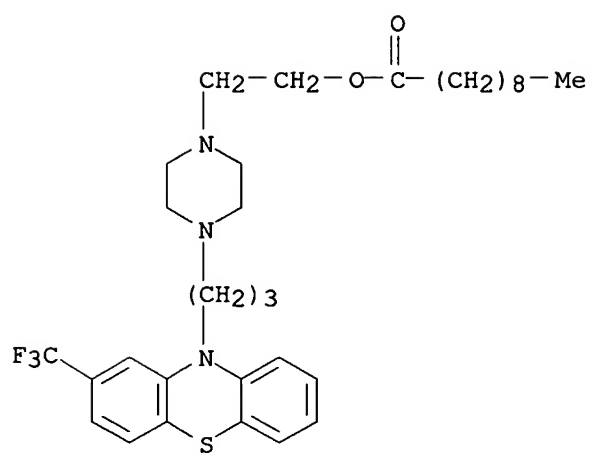
PRIORITY APPLN. INFO.:  
US 2002-389577P P 20020617  
US 2002-414831P P 20020927  
WO 2003-US19595 A1 20030617  
US 2004-13969 A2 20041216

AB The invention is disclosed for the treatment of psoriasis in a human  
comprising the intralesional administration of a phenothiazine, preferably  
fluphenazine, to a psoriatic plaque in the patient.

IT 5002-47-1, Fluphenazine decanoate  
RL: PAC (Pharmacological activity); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(intralesional treatment of psoriasis)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-  
1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



41 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1026604 CAPLUS

DOCUMENT NUMBER: 143:279436

TITLE: Tricyclic antidepressants and substituted phenothiazines for the treatment of peripheral neuropathy

INVENTOR(S): Conforti, Jeffrey

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005209220	A1	20050922	US 2004-804419	20040319
PRIORITY APPLN. INFO.:			US 2004-804419	20040319

AB The invention centers around the treatment of peripheral neuropathy by administering to a symptomatic patient, especially one suffering pain and/or burning symptoms and especially in the legs or feet, and soles of the feet, a combination of two medications, a substituted phenothiazine, and a tricyclic antidepressant. The substituted phenothiazine potentiates the activity of, or acts synergistically with the tricyclic antidepressant, to provide relief that is otherwise not obtainable with one medication alone at reasonable dosage levels. The particular antidepressant may be imipramine (or analog thereof) and may be selected from the group consisting of the following well-known antidepressants: desipramine, imipramine, imipramine N-oxide, trimipramine, clomipramine, doxepin, amitriptyline, nortriptyline, protriptyline, and their pharmaceutically acceptable free forms, and acid addition salts and esters thereof. The second compound of the regimen is a substituted phenothiazine. Those preferred for use in the invention are selected from the group consisting of chlorpromazine hydrochloride, mesoridazine besylate, thioridazine hydrochloride, acetophenazine maleate, fluphenazine, fluphenazine hydrochloride, fluphenazine enanthate, fluphenazine decanoate, perphenazine, trifluoperazine hydrochloride, and their pharmaceutically acceptable free forms, and acid addition salts and esters thereof. Most preferred is fluphenazine hydrochloride. The most preferred combination of antidepressant and substituted phenothiazine for use is desipramine hydrochloride with fluphenazine hydrochloride. The substituted phenothiazine may be taken alone, i.e. not in combination with the antidepressant. For fluphenazine, a dosage level higher than the amount used in the combination may be required depending on the severity of the neuropathy.

IT 2746-81-8, Fluphenazine enanthate 5002-47-1,

Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

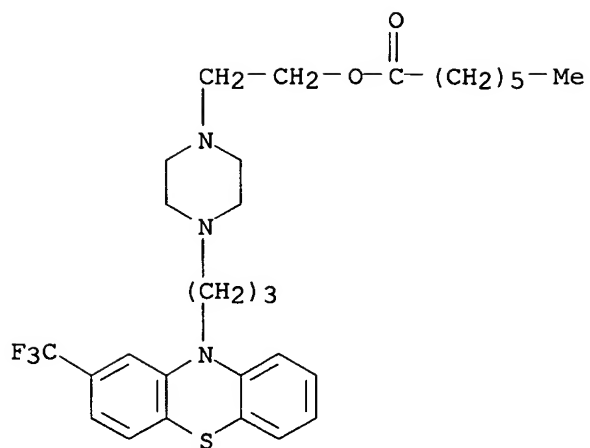
BIOL (Biological study); USES (Uses)

(tricyclic antidepressants and substituted phenothiazines for treatment of peripheral neuropathy)

RN 2746-81-8 CAPLUS

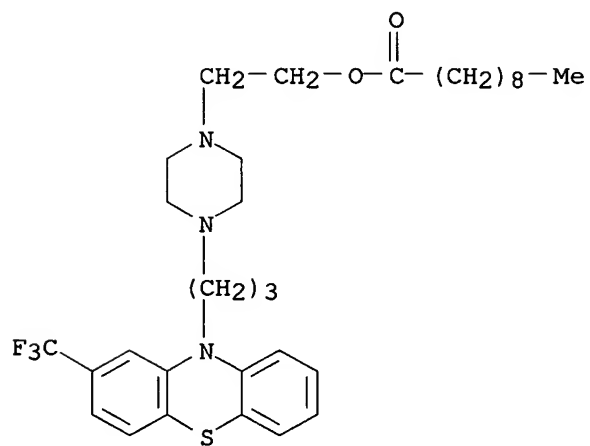
CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



141 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:798956 CAPLUS  
 DOCUMENT NUMBER: 143:452620  
 TITLE: Genomics revolution in contemporary psychiatric practices  
 AUTHOR(S): Razali, Salleh Mohd; Zalina, Zahari; Teh, Lay Kek; Rusli, Ismail  
 CORPORATE SOURCE: Department of Psychiatry, Universiti Sains Malaysia, Kelantan, 15990, Malay.  
 SOURCE: International Medical Journal (2005), 12(2), 117-123  
 CODEN: IMJOFS; ISSN: 1341-2051  
 PUBLISHER: Japan International Cultural Exchange Foundation  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Objective: To highlight the application of genomic technol. in drug development and therapy; and determine the frequency of 7 CYP2D6 alleles (CYP2D6 \*3, \*4, \*6, \*9, \*10, \*14, \*17) in schizophrenic patients and the relationship with treatment response. This is an early stage of identification of biol. predictors of drug efficacy. Materials and Methods: Reviewed of the relevant literatures in the area of pharmacogenetics and pharmacogenomics. Scrutinized the processes of identification of biol. predictors of drug efficacy in order to understand the mol. ingredient of antipsychotic drug response and adverse reactions. This is followed by a study that involves 65 schizophrenic patients. Results: Polymorphism of CYP2D6 would contribute to individual variations in response to antipsychotics. Since drug metabolism is determined by the number of

functional CYP2D6 gene present, genotyping of patients with CYP2D6 mutations or mutant alleles allows for safer choice of drug and better response to treatment. Thus, genotyping of schizophrenic patients on P 450 enzymes activity would be a predictor outcome in optimizing dosage to prevent side-effect of drug and achieve cost minimization of treatment. In relation to that the present study was conducted. Another pharmacogenetic study is being planned to evaluate the optimum dose of antipsychotic for individual patients. The study revealed that the only mutation detected among the schizophrenic subjects was CYP2D6\*10. The allele frequency of CYP2D6\*1 and CYP2D6\*10 were 78% and 40% resp. There were significant differences of the total PANNS score between CYP2D6\*10/CYP2D6\*10 and CYP2D6\*1/CYP2D6\*1 genotypes (Mann-Whitney U test,  $p = 0.039$ ), and between CYP2D6\*10/CYP2D6\*10 and CYP2D6\*1/CYP2D6\*10 genotypes ( $p = 0.017$ ); but no significant difference was noted between CYP2D6\*1/CYP2D6\*10 and CYP2D6\*1/CYP2D6\*1 genotypes. There was no significant relationship between CYP2D6 gene polymorphisms and treatment response. Conclusion: We have highlighted the application of pharmacogenomics technol. in the management of mental illness, which enable clinicians to tailor therapy of their patients on the basis of the unique genotype. This includes an identification of biol. predictor that involves a study on CYP2D6 polymorphisms in schizophrenia and response to the treatment, as part of the overall process of determining optimum dose of antipsychotic for individual patient. However, the study was inclusive due to small sample size and further study with bigger sample size and improved methodol. is needed. In the near future, genetic test could predict patient pharmacol. treatment response and vulnerability to a particular adverse effect.

IT 5002-47-1, Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

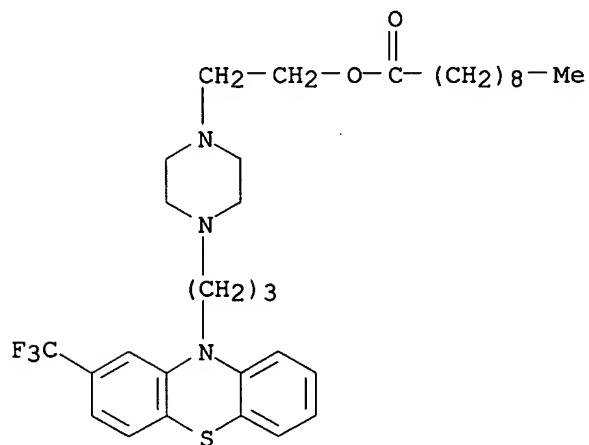
(CYP2D6\*10, CYP2D6\*1 genotype but not CYP2D6\*3, \*4, \*6, \*9, \*14, \*17)

10/808,541

genotype was detected and no relation between CYP2D6 poly  
treatment response was seen in schizophrenic patient treated  
antipsychotic fluphenazine decanoate)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]p  
1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

21

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

141 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:714045 CAPLUS

DOCUMENT NUMBER: 143:260172

TITLE: Thermoregulatory, motor, behavioural, and nociceptive responses of rats to 3 long-acting neuroleptics

AUTHOR(S): Fick, L. G.; Fuller, A.; Mitchell, D.

CORPORATE SOURCE: Brain Function Research Unit, School of Physiology, University of the Witwatersrand Medical School, Parktown, 2193, S. Afr.

SOURCE: Canadian Journal of Physiology and Pharmacology (2005), 83(6), 517-527

CODEN: CJPPA3; ISSN: 0008-4212

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated physiol. effects of i.m. injections of the following 3 long-acting neuroleptics commonly used in wildlife management: haloperidol (0.05, 0.1, and 0.5 mg/kg body mass), zuclopenthixol acetate (0.5, 1, and 5 mg/kg), and perphenazine enanthate (1, 3, and 10 mg/kg), in a rat model. Body temperature and cage activity were measured by intra-abdominal telemeters. Nociceptive responses were assessed by challenges to noxious heat and pressure. Haloperidol (0.5 mg/kg) produced a significant nocturnal hypothermia ( $p < 0.05$ ) and decreased night-time cage activity and food intake. Zuclopenthixol (5 mg/kg) significantly decreased nighttime body temperature and cage activity and, at 1 mg/kg and 5 mg/kg, significantly decreased food intake 5-17 h after injection ( $p < 0.05$ ). Perphenazine (10 mg/kg) significantly decreased nighttime body temperature and cage activity

and,

at all doses, significantly decreased food intake 5-17 h after injection ( $p < 0.05$ ). Significant analgesic activity was evident in rats given 5 mg/kg zuclopenthixol up to 40 h after injection, and 10 mg/kg perphenazine from 48 to 96 h after injection ( $p < 0.0001$ ). Zuclopenthixol (5 mg/kg) and perphenazine (10 mg/kg) had significant antihyperalgesic activities at 16 h postinjection and 24-48 h postinjection, resp. ( $p < 0.0001$ ). Haloperidol had no significant antinociceptive activity at doses tested. Motor function was impaired in rats given 0.5 mg/kg haloperidol, 5 mg/kg zuclopenthixol and 10 mg/kg perphenazine. Effects of long-acting neuroleptics on body temperature, feeding, and activity were short-lasting and should not preclude their use in wildlife. Antinociceptive actions were longer-lasting, but were nonspecific, and we recommend addnl. analgesics for painful procedures during wildlife management.

IT 17528-28-8, Perphenazine enanthate

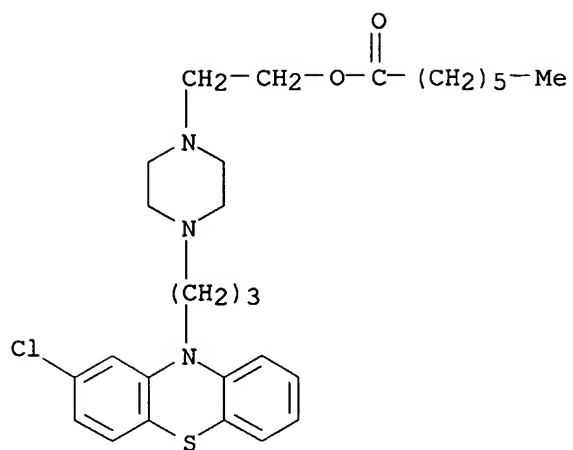
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(thermoregulatory, motor, behavioral, and nociceptive responses of rats to 3 long-acting neuroleptics)

RN 17528-28-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

49

THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/808,541

111 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:471959 CAPLUS

DOCUMENT NUMBER: 143:1313

TITLE: Use of cyclooxygenase-2 selective inhibitors and combinations with neuroleptics for the treatment of schizophrenic disorders

INVENTOR(S): Hagan, James; Routledge, Carol

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049034	A2	20050602	WO 2004-EP13076	20041117
WO 2005049034	A3	20050922		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

GB 2003-26967

A 20031119

GB 2003-27937

A 20031202

OTHER SOURCE(S): MARPAT 143:1313

AB The invention discloses the use of compds. which are cyclooxygenase-2 (COX-2) inhibitors, and pharmaceutically acceptable salts and solvates thereof, for the treatment of schizophrenic disorders. Schizophrenic disorders of the invention are to be intended schizophrenia, delusional disorders, affective disorders, autism or tic disorders, schizophreniform disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders. Moreover, the invention discloses the use of a pyrimidine derivative known as a COX-2 inhibitor in combination with a neuroleptic drug for the treatment of schizophrenic disorders. Compound preparation is described.

IT 2746-81-8, Fluphenazineenanthate 5002-47-1, Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

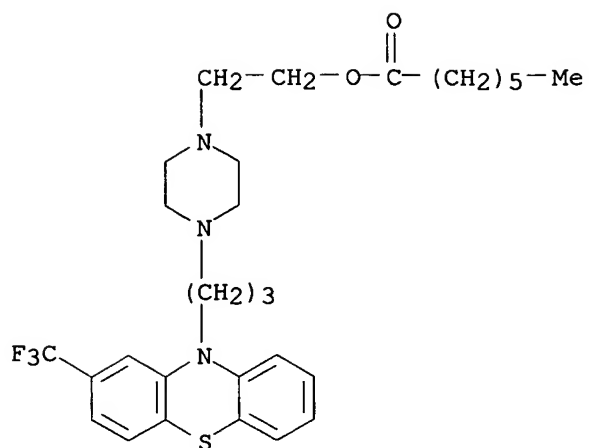
BIOL (Biological study); USES (Uses)

(cyclooxygenase-2 inhibitors and combinations with neuroleptics for treatment of schizophrenic disorders)

RN 2746-81-8 CAPLUS

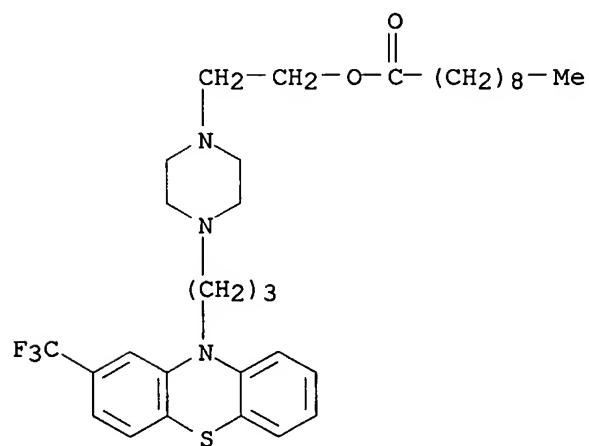
CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

10/808,541



RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



~~141~~ ANSWER 8 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:309155 CAPLUS

DOCUMENT NUMBER: 142:475958

TITLE: A 6-month, placebo-controlled trial of D-cycloserine co-administered with conventional antipsychotics in schizophrenia patients

AUTHOR(S): Goff, Donald C.; Herz, Lawrence; Posever, Thomas; Shih, Vivian; Tsai, Guochuan; Henderson, David C.; Freudenreich, Oliver; Evins, A. Eden; Yovel, Iftah; Zhang, Hui; Schoenfeld, David

CORPORATE SOURCE: Schizophrenia Program, Massachusetts General Hospital, Boston, MA, USA

SOURCE: Psychopharmacology (Berlin, Germany) (2005) 179(1), 144-150

CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB D-Cycloserine, a partial agonist at the glycine site of the N-methyl-D-aspartate receptor, has demonstrated inconsistent efficacy for neg. and cognitive symptoms of schizophrenia. The strongest evidence for efficacy has come from studies using D-cycloserine at a dose of 50 mg/day added to conventional antipsychotics in trials of 8 wk duration or less. Objective: To assess the efficacy for neg. symptoms and cognitive impairment of D-cycloserine augmentation of conventional antipsychotics in a 6-mo trial. Fifty-five schizophrenia patients with prominent neg. symptoms, treated with conventional antipsychotics, were randomly assigned to treatment with D-cycloserine 50 mg/day or placebo for 6 mo in a double-blind, parallel group design. Twenty-six subjects completed the 6-mo trial; drop-out rates did not differ between treatment groups. D-Cycloserine treatment did not differ from placebo treatment on any primary outcome measure at 8 or 24 wk, including response of neg. symptoms and performance on a cognitive battery. Serum D-cycloserine concns. did not correlate with response of neg. symptoms. D-Cycloserine did not exhibit therapeutic effects in this trial, possibly reflecting the high drop-out rate, a narrow range of therapeutic serum concns., a modest magnitude of therapeutic effect for the selected outcome measures, or loss of efficacy over time. Because D-cycloserine is a partial agonist with relatively low affinity for the glycine site, the magnitude of potential therapeutic effect may be smaller than that achieved by the higher-affinity full agonists, glycine and D-serine.

IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); PAC

(Pharmacological activity); THU (Therapeutic use); BIOL

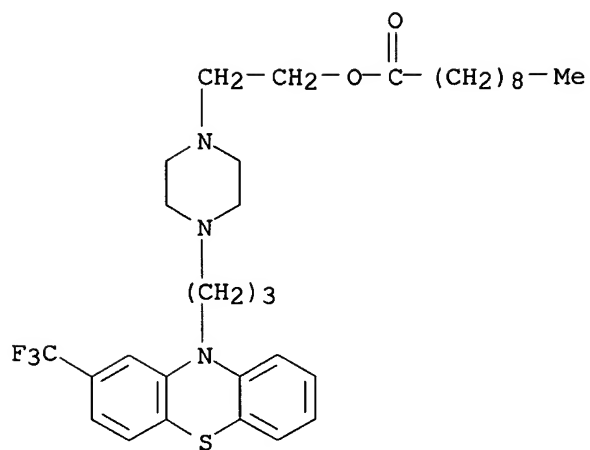
(Biological study); USES (Uses)

(efficacy of D-cycloserine co-administered with conventional antipsychotics for neg. symptoms and cognitive impairment in schizophrenia patients)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT:

37

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/808,541

L41 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:283298 CAPLUS

DOCUMENT NUMBER: 142:349042

TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms

INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzen; Keith, Curtis

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004273910	A1	20050331	AU 2004-273910	20040916
CA 2538570	AA	20050331	CA 2004-2538570	20040916
EP 1670477	A2	20060621	EP 2004-788798	20040916
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
PRIORITY APPLN. INFO.:			US 2003-504310P	P 20030918
			WO 2004-US30368	W 20040916

OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT 84-06-0, Thiopropazate

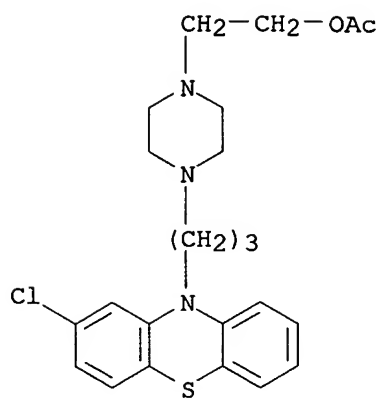
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(chlorpromazine compound-antiproliferative drug antitumor combination)

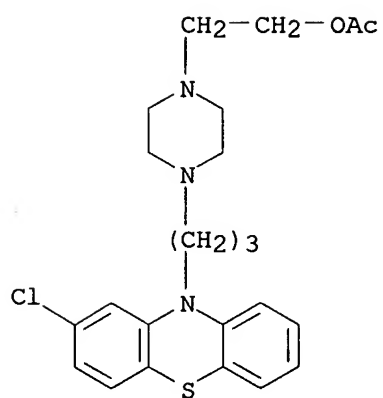
RN 84-06-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)



~~141~~ ANSWER 10 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:216611 CAPLUS  
 DOCUMENT NUMBER: 142:291340  
 TITLE: Formulations, conjugates, and combinations of drugs  
 for the treatment of neoplasms  
 INVENTOR(S): Nichols, James M.; Foley, Michael A.; Keith, Curtis;  
 Padval, Mahesh; Elliott, Peter  
 PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA  
 SOURCE: PCT Int. Appl., 92 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020913	A2	20050310	WO 2004-US27695	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005080075	A1	20050414	US 2004-925835	20040825
PRIORITY APPLN. INFO.:			US 2003-497617P	P 20030825
OTHER SOURCE(S): MARPAT 142:291340				
AB The invention provides formulations and structural modifications for phenothiazine compds. which result in altered biodistribution, thereby reducing the occurrence of adverse reactions associated with this class of drug.				
IT 84-06-0, Thiopropazate RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (formulations and conjugates and combinations of drugs such as phenothiazines for treatment of neoplasms with decreased penetration of blood-brain barrier and CNS effects)				
RN 84-06-0 CAPLUS				
CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)				



10/808,541

L42 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1122248 CAPLUS

DOCUMENT NUMBER: 142:403960

TITLE: Switching depot antipsychotic drug responders to oral olanzapine

AUTHOR(S): Godleski, Linda S.; Goldsmith, L. Jane; Vieweg, W. Victor R.; Zettwoch, Nancy; Stikovac, Dejzi; Lewis, Susan

CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Louisville, KY, USA

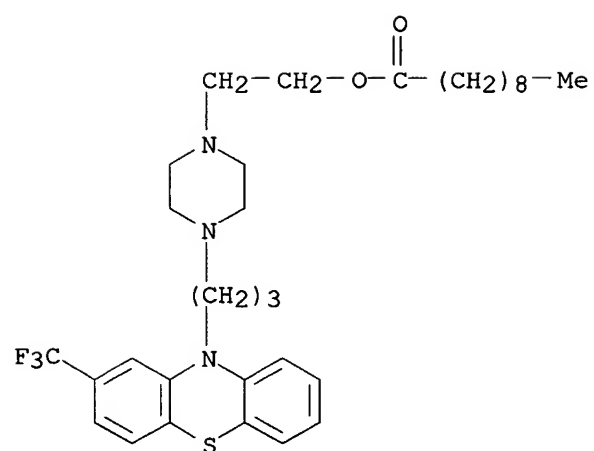
SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (2005), 28(1), 141-144  
CODEN: PNPD7; ISSN: 0278-5846

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

- AB In an open-label study, 13 patients taking depot antipsychotic medication for greater than 3 years were switched to oral olanzapine. The first 3-mo experience has been previously reported. We now describe a second 3-mo experience and integrate our observations into a cumulative 6-mo report. Monthly, we assessed patients using clin. ratings [Pos. and Neg. Syndrome Scale (PANSS), Global Assessment of Functioning (GAF), Mini-Mental State Exam (MMSE), and Clin. Global Improvement Scale (CGI)] and side effect parameters [Abnormal Involuntary Movement Scale (AIMS), Association for Methodol. and Documentation in Psychiatry psychotropic side effect rating scale (AMDP-5), and wts.]. Olanzapine patients showed statistically significant improvement (baseline to endpoint sixth month) in GAF ( $p=0.015$ ), MMSE ( $p=0.022$ ), CGI improvement, and AIMS ( $p=0.038$ ). There was no statistically significant change in PANSS, CGI severity, or AMDP-5 overall side effects. Weight gain over 6 mo averaged 8.9 lb. All patients completed the study. Compliance was estimated at 90%, and 81% of patients chose to continue on the oral olanzapine. One patient was hospitalized at the conclusion of the study. Our findings suggest that clinicians may consider oral olanzapine as a viable alternative to depot antipsychotic medications, balancing clin. improvement in some clin. measures with lack of improvement in other clin. measures; and balancing improvement in abnormal involuntary movements with weight gain and its sequelae.
- IT 5002-47-1, Fluphenazine decanoate  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(switching depot antipsychotic drug fluphenazine decanoate to olanzapine showed marked clin. improvement in GAF, MMSE, AIMS while no change in PANSS, CGI severity, AMDP-5 overall side effects but with weight gain in schizophrenia patient)
- RN 5002-47-1 CAPLUS
- CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

16

THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

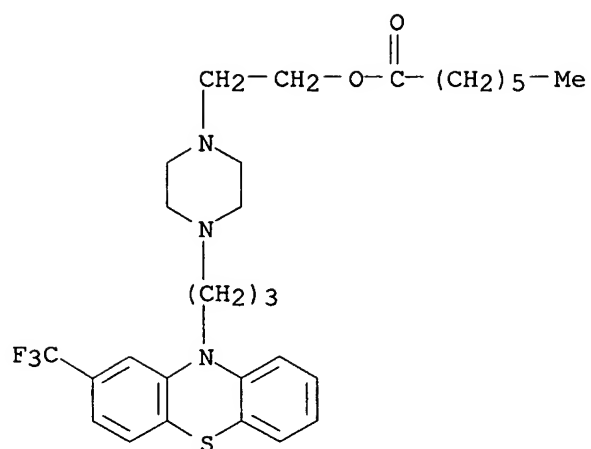
L41 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN  
 X ACCESSION NUMBER: 2004:1019878 CAPLUS  
 DOCUMENT NUMBER: 142:731  
 TITLE: Use of secretin in treatments of disorders associated with the amygdala  
 INVENTOR(S): Yurgelun-Todd, Deborah A.; Renshaw, Perry F.  
 PATENT ASSIGNEE(S): The McLean Hospital Corporation, USA  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100899	A2	20041125	WO 2004-US15282	20040513
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2003-470177P P 20030513

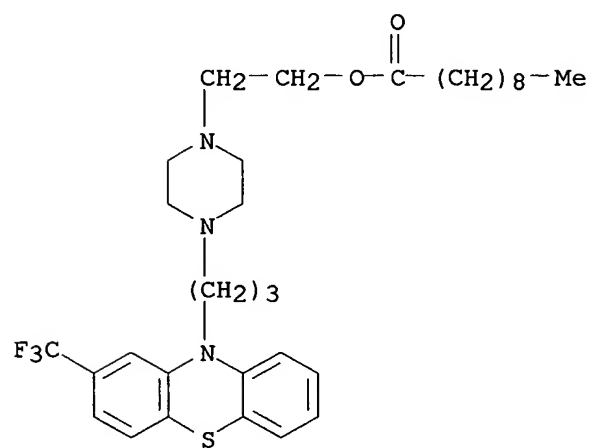
AB The invention provides methods for treating disorders associated with the amygdala. The methods of treatment are based on the administration of a therapeutically effective amount of secretin to an individual suffering from a disorder associated with the amygdala, e.g., bipolar disorder or a substance use disorder.  
 IT 2746-81-8, Fluphenazine enanthate 5002-47-1, Fluphenazine decanoate  
 RL: PAC (Pharmacological activity); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (use of secretin in treatments of disorders associated with amygdala)  
 RN 2746-81-8 CAPLUS  
 CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:995776 CAPLUS

DOCUMENT NUMBER: 141:406120

TITLE: Compositions and methods for the treatment of parkinson's disease and tardive dyskinesias with quinoline ring-containing neuromelanin-binding compounds

INVENTOR(S): Nelson, Jodi

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 192,414.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229908	A1	20041118	US 2003-616692	20030709
US 6417177	B1	20020709	US 2000-615639	20000713
US 2002198231	A1	20021226	US 2002-192414	20020709
PRIORITY APPLN. INFO.:			US 1999-143767P	P 19990713
			US 2000-175051P	P 20000107
			US 2000-202140P	P 20000505
			US 2000-615639	A2 20000713
			US 2002-192414	A2 20020709
			US 2003-479748P	P 20030619

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having

a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine diphosphate. Selected adjuvants are also provided as part of the compns. of this invention.

IT 5002-47-1, Fluphenazine decanoate

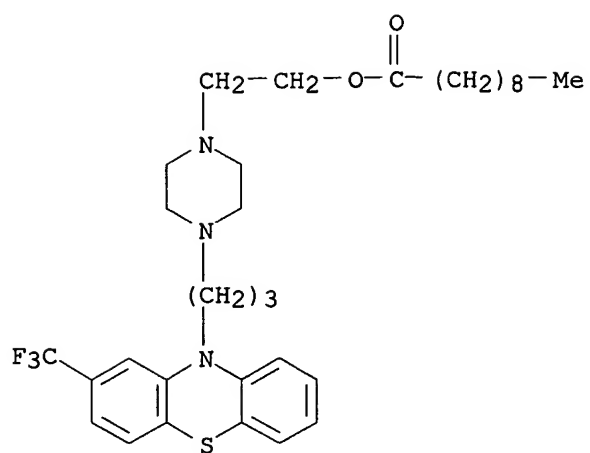
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



141 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:959435 CAPLUS

DOCUMENT NUMBER: 142:232281

TITLE: Haloperidol Half-life After Chronic Dosing

AUTHOR(S): de Leon, Jose; Diaz, Francisco J.; Wedlund, Peter; Josiassen, Richard C.; Cooper, Thomas B.; Simpson, George M.

CORPORATE SOURCE: Mental Health Research Center at Eastern State Hospital, Lexington, KY, USA

SOURCE: Journal of Clinical Psychopharmacology (2004), 24(6), 656-660

CODEN: JCPYDR; ISSN: 0271-0749

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In normal subjects after a single oral dose, haloperidol half-life has been reported to range 14.5-36.7 h (or up to 1.5 days). After chronic administration, half-lives of up to 21 days have been reported. The objective of this study was to evaluate specific factors that might account for differences in haloperidol half-life in patients taking haloperidol chronically, including gender, age, weight, race, CYP2D6 and CYP3A5 genotypes, comedication, and smoking. Thirty-one patients were administered haloperidol for 4 wk followed by a 1-wk washout before administration of clozapine. Haloperidol plasma levels were measured weekly for at least 2 mo after discontinuation. The geometric mean for haloperidol half-life and detectable levels duration were 3.9 and 13.8 days, resp. Within 31 subjects, 58% (18/31) had half-lives <3 days (1.2-2.3 days) and 42% (13/31) had half-lives ≥3 days. Two of 3 patients with half-lives longer than 30 days (720 h) and levels detectable >2 mo had received haloperidol decanoate. Five patients who received haloperidol decanoate in the prior year were excluded from a comparison between patients with long haloperidol half-lives (≥3 days, n = 10) and patients with short half-lives (<3 days, n = 16). The only significant difference between the two groups was that African-Americans (n = 4) were all found to have a long haloperidol half-life (P = 0.014). CYP3A5 genotype did not appear to influence haloperidol half-life but the two CYP2D6 poor metabolizer had half-lives ≥3 days. This study suggests that haloperidol half-life following repeated drug administration is substantially more prolonged than what has been observed after acute haloperidol administration.

IT 5002-47-1, Fluphenazine decanoate

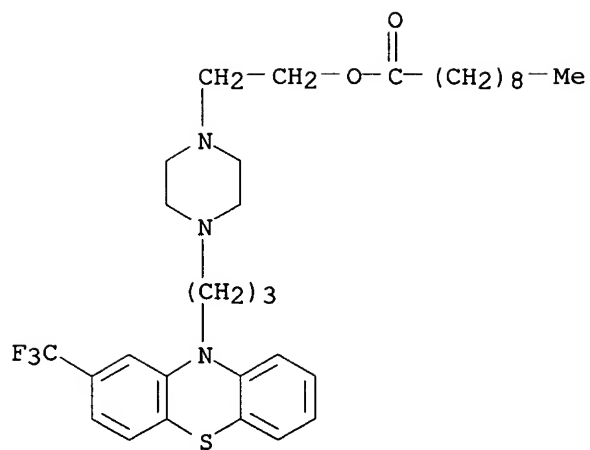
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(haloperidol half life after chronic dosing was prolonged with no association with gender, age, body weight, genotyping, comedication with fluphenazine decanoate or smoking)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

21

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:453015 CAPLUS

DOCUMENT NUMBER: 141:17632

TITLE: Methods and agents elevating cAMP and calcium ion for increasing neurogenesis

INVENTOR(S): Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestr nd, Anders; Heidrich, Jessica; Hellstrom, Kristina; Haggblad, Johan; Jansson, Katarina; Kortessmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jacqueline; Mercer, Alex; Njberg, Karl; Ossoinak, Amina; Patrone, Cesare; Ronnholm, Harriet; Zachrisson, Olof; Wikstrom, Lilian

PATENT ASSIGNEE(S): Neuronova AB, Swed.

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
WO 2004045592	A3	20041104		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2506850	AA	20040603	CA 2003-2506850	20031120
AU 2003280117	A1	20040615	AU 2003-280117	20031120
EP 1583541	A2	20051012	EP 2003-772495	20031120
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006514630	T2	20060511	JP 2004-553032	20031120
WO 2005081619	A2	20050909	WO 2004-IB4451	20041119
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2002-427912P	P 20021120
			US 2003-718071	A 20031120
			WO 2003-IB5311	W 20031120
			US 2004-850055	A 20040519

AB The invention discloses methods for promoting neurogenesis by contacting neuronal tissue with intracellular cAMP-elevating agents and intracellular

calcium ion-elevating agents. Agents for promoting neurogenesis are also disclosed.

IT 2746-81-8 5002-47-1

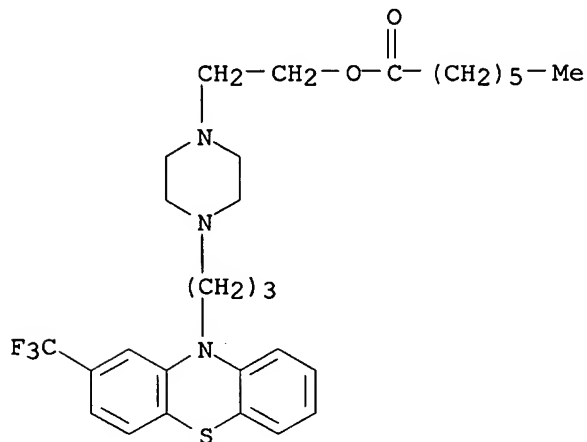
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(cAMP-elevating and calcium ion-elevating compds. for increasing neurogenesis)

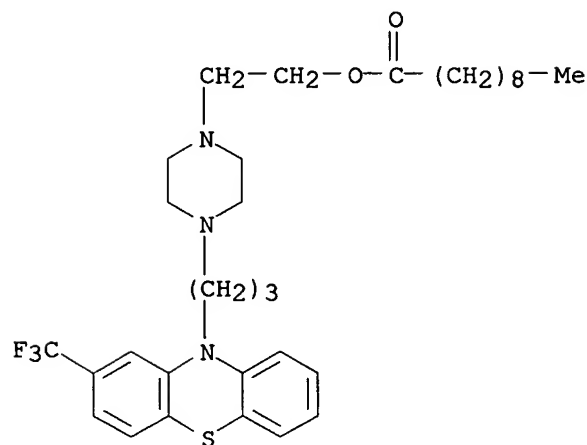
RN 2746-81-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



10/808,541

LAN ANSWER 16 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:393436 CAPLUS

DOCUMENT NUMBER: 140:385938

TITLE: Stress in wild-caught Eurasian otters (*Lutra lutra*):  
Effects of a long-acting neuroleptic and time in  
captivity

AUTHOR(S): Fernandez-Moran, J.; Saavedra, D.; De La Torre, J. L.  
Ruiz; Manteca-Villanova, X.

CORPORATE SOURCE: Veterinary Service, Barcelona Zoo, Barcelona, 08003,  
Spain

SOURCE: Animal Welfare (2004), 13(2), 143-149

CODEN: ANWEEF; ISSN: 0962-7286

PUBLISHER: Universities Federation for Animal Welfare

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As part of a translocation project, 28 Eurasian otters (*Lutra lutra*) were captured from the wild and transported to the Barcelona Zoo for veterinary evaluation, quarantine and i.p. implantation of telemetry devices. Eleven animals were injected with the long-acting neuroleptic (LAN) perphenazine enanthate at the time of capture and the remaining animals served as a control group. During their time in captivity, which averaged 23 days, all of the animals were bled three times. Haematol. and biochem. parameters were evaluated, including red blood cell count (RBC), Hb (Hb), white blood cell count (WBC), blood urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), lactate dehydrogenase (LDH), creatine kinase (CK), albumin, and serum cortisol. No significant differences were found between treated and control otters except for monocyte count, which was higher in treated animals. Time after capture had an effect on many parameters. RBC and Hb decreased at first and then increased, while WBC and segmented neutrophils decreased over time. Most of the biochem. parameters considered to vary in relation to stress, including AST, ALT, CK, AP and LDH, decreased over time, suggesting that the stress responses of the animals decreased throughout the period of captivity. However, no significant change in serum cortisol levels was noted. The lack of effect of perphenazine treatment on haematol. parameters should encourage further research on other stress indicators applicable to wild animals, such as behavior or faecal cortisol concentration. Finally, the results obtained in this study suggest that, when captive conditions are adequate, keeping wild-caught animals in human care for a period of time prior to their release into the wild can be beneficial. However, further studies taking into account other welfare indicators would be useful.

IT 17528-28-8, Perphenazine enanthate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

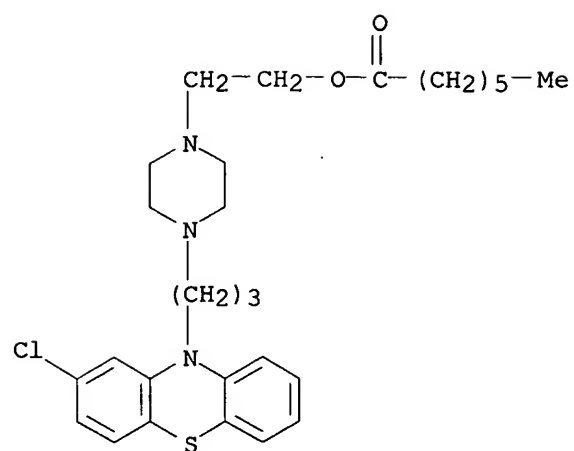
BIOL (Biological study); USES (Uses)

(effects of a long-acting neuroleptic and time in captivity on stress  
in wild-caught Eurasian otters)

RN 17528-28-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-  
piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT:

43

THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:214183 CAPLUS

DOCUMENT NUMBER: 141:271350

TITLE: Glycine transporter I inhibitor, N-Methylglycine (sarcosine), added to antipsychotics for the treatment of schizophrenia

AUTHOR(S): Tsai, Guochuan; Lane, Hsien-Yuan; Yang, Pinchen; Chong, Mian-Yoon; Lange, Nicholas

CORPORATE SOURCE: Laboratory of Molecular and Psychiatric Neuroscience, McLean Hospital and Harvard Medical School, Boston, MA, USA

SOURCE: Biological Psychiatry (2004), 55(5), 452-456

CODEN: BIPCBF; ISSN: 0006-3223

PUBLISHER: Elsevier Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: ypofunction of N-methyl-D-aspartate glutamate receptor had been implicated in the pathophysiol. of schizophrenia. Treatment with D-serine or glycine, endogenous full agonists of the glycine site of N-methyl-D-aspartate receptor, or D-cycloserine, a partial agonist, improve the symptoms of schizophrenia. N-methylglycine (sarcosine) is an endogenous antagonist of glycine transporter-1, which potentiates glycine's action on N-methyl-D-aspartate glycine site and can have beneficial effects on schizophrenia. Methods: Thirty-eight schizophrenic patients were enrolled in a 6-wk double-blind, placebo-controlled trial of sarcosine (2 g/d), which was added to their stable antipsychotic regimens. Twenty of them received risperidone. Measures of clin. efficacy and side effects were determined every other week. Results: Patient who received sarcosine treatment revealed significant improvements in their pos., neg., cognitive, and general psychiatric symptoms. Similar therapeutic effects were observed when only risperidone-treated patients were analyzed. Sarcosine was well-tolerated, and no significant side effect was noted. Conclusions: Sarcosine treatment can benefit schizophrenic patients treated by antipsychotics including risperidone. The significant improvement with the sarcosine further supports the hypothesis of N-methyl-D-aspartate receptor hypofunction in schizophrenia. Glycine transporter-1 is a novel target for the pharmacotherapy to enhance N-methyl-D-aspartate function.

IT 5002-47-1, Fluphenazine decanoate

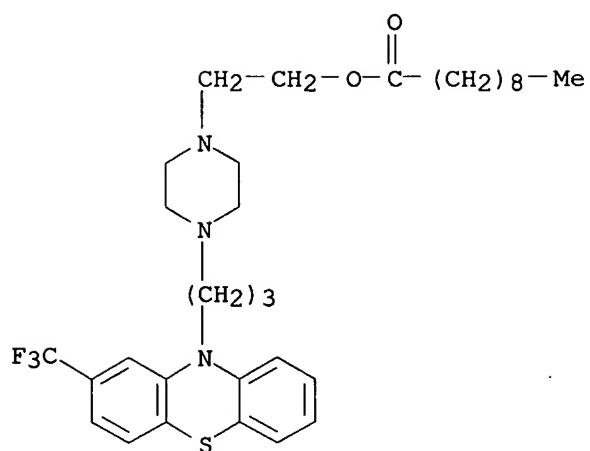
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(sarcosine added to antipsychotic fluphenazine decanoate including risperidone was well-tolerated, improved pos., neg., cognitive, other psychiatric symptoms, used as therapeutic agent for treatment of patient with schizophrenia)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

41

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/808,541

141 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60249 CAPLUS  
DOCUMENT NUMBER: 140:122767  
TITLE: Pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms  
INVENTOR(S): Borisy, Alexis; Keith, Curtis; Foley, Michael A.; Stockwell, Brent R.; Gaw, Debra A.; Nichols, M. James; Lee, Margaret S.  
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA  
SOURCE: PCT Int. Appl., 76 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006842	A2	20040122	WO 2003-US21803	20030711
WO 2004006842	A3	20040527		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2492059	AA	20040122	CA 2003-2492059	20030711
AU 2003256511	A1	20040202	AU 2003-256511	20030711
US 2004116407	A1	20040617	US 2003-617424	20030711
BR 2003012597	A	20050510	BR 2003-12597	20030711
EP 1545544	A2	20050629	EP 2003-764557	20030711
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1681511	A	20051012	CN 2003-821151	20030711
JP 2005536509	T2	20051202	JP 2004-521730	20030711
NO 2005000204	A	20050408	NO 2005-204	20050113
PRIORITY APPLN. INFO.:			US 2002-395233P	20020711
			WO 2003-US21803	20030711

OTHER SOURCE(S): MARPAT 140:122767

AB The invention features a method for treating a patient having a cancer or other neoplasm by administering to the patient pentamidine (or an analog thereof) and chlorpromazine (or an analog thereof) simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT 84-06-0, Thiopropazate

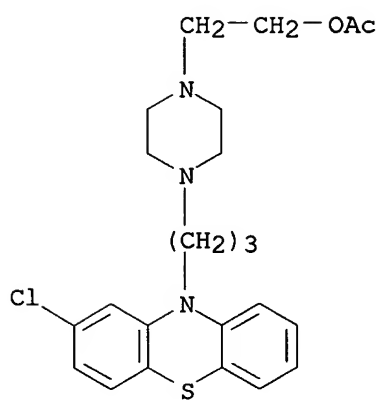
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

RN 84-06-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)



L41 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:41228 CAPLUS

DOCUMENT NUMBER: 140:105304

TITLE: Compositions and methods for the treatment of Parkinson's disease and tardive dyskinesias

INVENTOR(S): Nelson, Jodi

PATENT ASSIGNEE(S): Alpha Research Group, L.L.C., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004660	A2	20040115	WO 2003-US21463	20030709
WO 2004004660	A3	20051103		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2002198231	A1	20021226	US 2002-192414	20020709
CA 2531810	AA	20040115	CA 2003-2531810	20030709
AU 2003248893	A1	20040123	AU 2003-248893	20030709
EP 1581167	A2	20051005	EP 2003-763398	20030709
EP 1581167	A3	20051221		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006514917	T2	20060518	JP 2004-520071	20030709
PRIORITY APPLN. INFO.:			US 2002-192414	A 20020709
			US 2003-479748P	P 20030619
			US 1999-143767P	P 19990713
			US 2000-175051P	P 20000107
			US 2000-202140P	P 20000505
			US 2000-615639	A2 20000713
			WO 2003-US21463	W 20030709

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having

a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine diphosphate. Selected adjuvants are also provided as part of the compns. of this invention.

IT 5002-47-1, Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

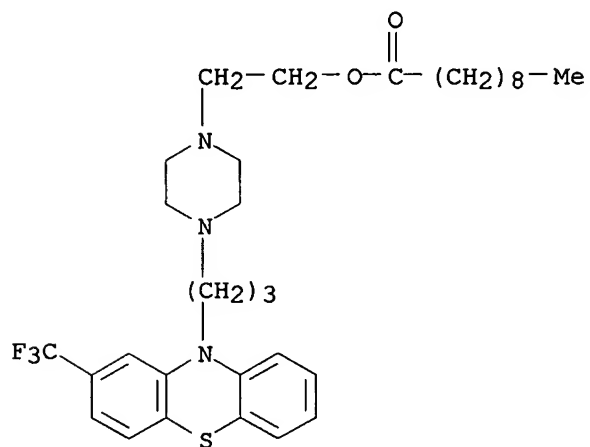
BIOL (Biological study); USES (Uses)

10/808,541

(comps. for treatment of Parkinson's disease and tardive dyskinesias)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



141 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:904480 CAPLUS

DOCUMENT NUMBER: 140:349951

TITLE: Chlorpromazine equivalents versus defined daily doses: how to compare antipsychotic drug doses?

AUTHOR(S): Rijcken, Claudia A. W.; Monster, Taco B. M.; Brouwers, Jacobus R. B. J.; de Jong-van den Berg, Lolkje T. W.

CORPORATE SOURCE: Department of Social Pharmacy, Pharmacoepidemiology, and Pharmacotherapy, Groningen University Institute of Drug Exploration, Groningen, Neth.

SOURCE: Journal of Clinical Psychopharmacology (2003), 23(6), 657-659

CODEN: JCPYDR; ISSN: 0271-0749

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Classic chlorpromazine (CPZ) equivalent can be used to chart relative antipsychotic potencies of antipsychotic drugs. Values of CPZ equivalent per drug are ambiguous in literature. In drug use evaluation studies, antipsychotic doses are frequently compared by use of the defined daily dose (DDD). The DDD is the assumed average maintenance dose per day for a drug if used for its main indication in adults. The DDD is based on review of the available older and recent literature. In this report, we evaluated discrepancy between CPZ-equivalent values and DDD-equivalent values.

We plotted CPZ-equivalent values against DDD-equivalent values and performed linear regression to determine the mean relationship between the 2 methods. About 67% of the DDD-equivalent values demonstrated lower potencies for antipsychotic drug compared with CPZ-equivalent values. The slope of the regression line was 0.68 ( $r^2 = 0.81$ ). Because we found a great discrepancy between these 2 methods of comparing antipsychotic drug doses, we think further research is necessary to develop a standardized way of antipsychotic drug comparison.

IT 84-06-0, Thiopropazate

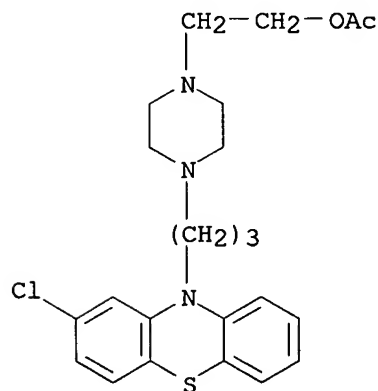
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(chlorpromazine equivalent vs. defined daily doses of antipsychotic drugs)

RN 84-06-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)





10/808,541

REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~L41~~ ANSWER 21 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN  
 X ACCESSION NUMBER: 2003:532347 CAPLUS  
 X DOCUMENT NUMBER: 139:79173  
 TITLE: Methods and compositions using a cyclooxygenase 2  
 (COX-2) inhibitor for the treatment of psychiatric  
 disorders  
 INVENTOR(S): Muller, Norbert  
 PATENT ASSIGNEE(S): Germany  
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

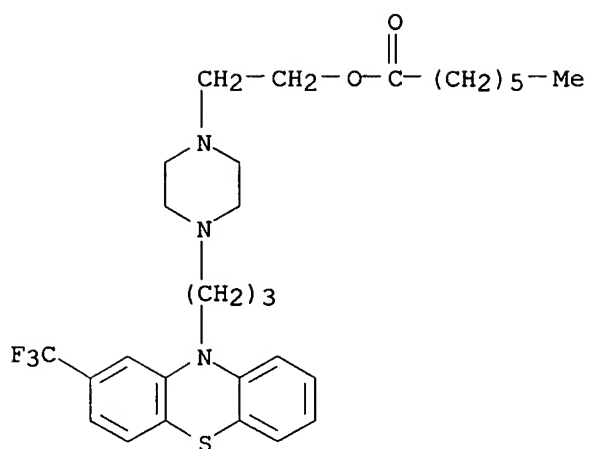
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130334	A1	20030710	US 2002-157969	20020531
EP 1627639	A2	20060222	EP 2005-24864	20020531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			DE 2001-10129328	A 20010619
			US 2002-364904P	B 20020314
			DE 2001-10129320	A 20010619
			EP 2002-738138	A3 20020531

OTHER SOURCE(S): MARPAT 139:79173

AB A method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia, is described which comprises administering a COX-2 inhibitor, or prodrug thereof, to a subject. Moreover, a method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia or a depressive disorder, is disclosed, comprising administering to a subject a COX-2 inhibitor or prodrug thereof in combination with a neuroleptic drug or an antidepressant. Compns. and kits that are suitable for the practice of the method are also described.

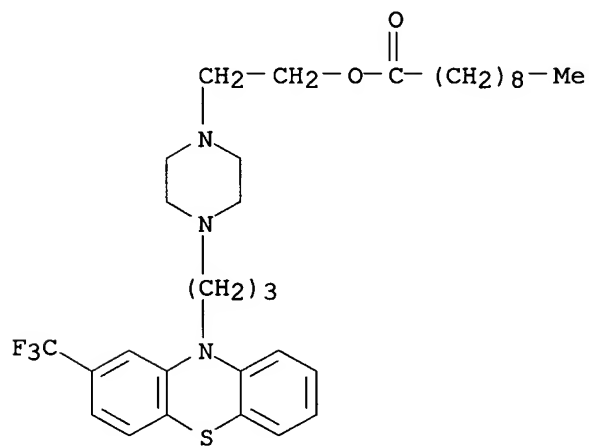
IT 2746-81-8, Fluphenazine enanthate 5002-47-1,  
 Fluphenazine decanoate  
 RL: PAC (Pharmacological activity); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (cyclooxygenase 2 inhibitor for treatment of psychiatric disorders, and use with other agents)

RN 2746-81-8 CAPLUS  
 CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

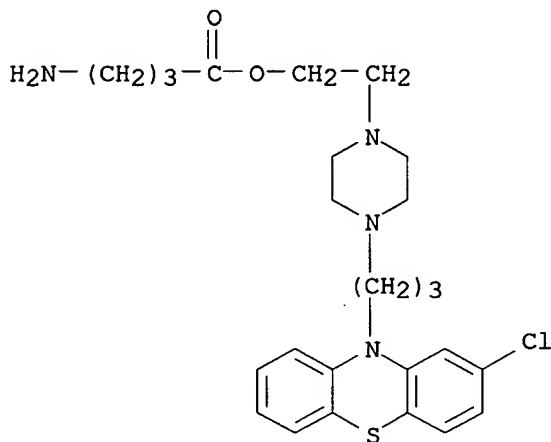


L41 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:261599 CAPLUS  
 DOCUMENT NUMBER: 138:265698  
 TITLE: Organic acid-conjugated antipsychotic drugs, and  
 therapeutic use thereof  
 INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada; Gil-Ad, Irit;  
 Weizman, Abraham  
 PATENT ASSIGNEE(S): Ramot at Tel Aviv University Ltd., Israel; Bar Ilan  
 University  
 SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026563	A2	20030403	WO 2002-IL795	20020929
WO 2003026563	A3	20040318		
WO 2003026563	C2	20040422		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2461663	AA	20030403	CA 2002-2461663	20020929
EP 1429844	A2	20040623	EP 2002-772790	20020929
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005503423	T2	20050203	JP 2003-530202	20020929
CN 1596141	A	20050316	CN 2002-823600	20020929
AU 2004201240	A1	20040506	AU 2004-201240	20040325
US 2004242570	A1	20041202	US 2004-808541	20040325
WO 2005092392	A2	20051006	WO 2005-IL341	20050327
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2001-324936P	P 20010927
			WO 2002-IL795	W 20020929
			US 2004-808541	A 20040325
AB	Chemical conjugates of anti-psychotic drugs and organic acids, uses thereof in the treatment of psychotic and/or proliferative disorders and diseases and as chemosensitizing agents, and their syntheses, are disclosed. The organic acids are selected to reduce side effects induced by the anti-psychotic			

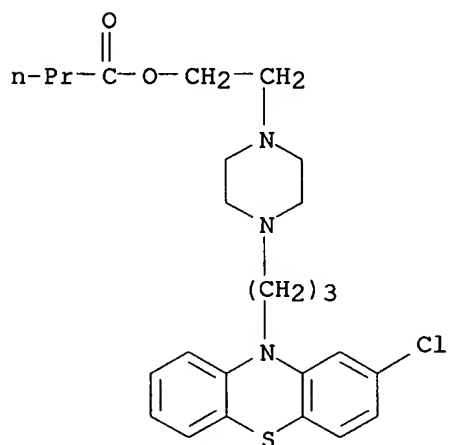
10/808,541

drugs and/or to exert an anti-proliferative activity.  
IT 503537-33-5P 503569-71-9P, AN 167  
RL: ADV (Adverse effect, including toxicity); PAC  
(Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation);  
USES (Uses)  
(organic acid-conjugated antipsychotic drugs, and therapeutic use)  
RN 503537-33-5 CAPLUS  
CN Butanoic acid, 4-amino-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-  
1-piperazinyl]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 503569-71-9 CAPLUS  
CN Butanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-  
piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



IT 1063-36-1P, AN 181 503569-70-8P, AN 130

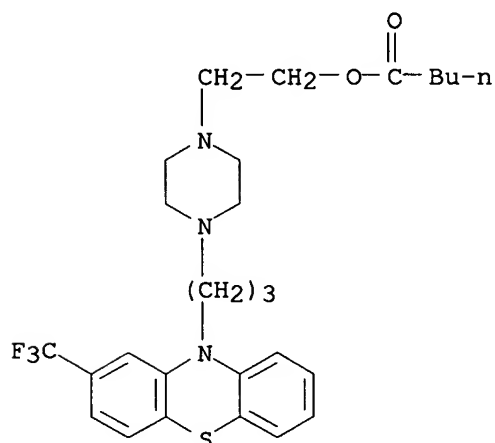
503569-72-0P, AN 177 503569-73-1P 503569-74-2P  
 , AN 179 503569-75-3P, AN 187

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

(organic acid-conjugated antipsychotic drugs, and therapeutic use)

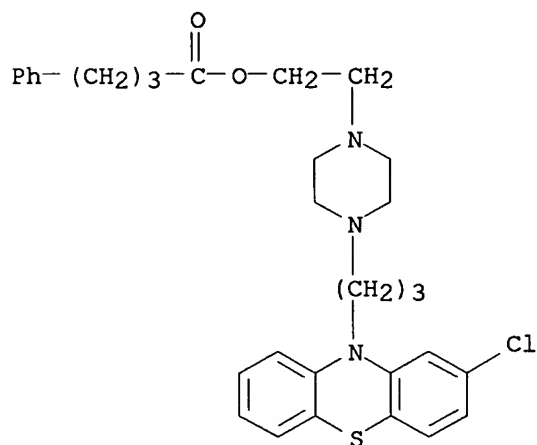
RN 1063-36-1 CAPLUS

CN Pentanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



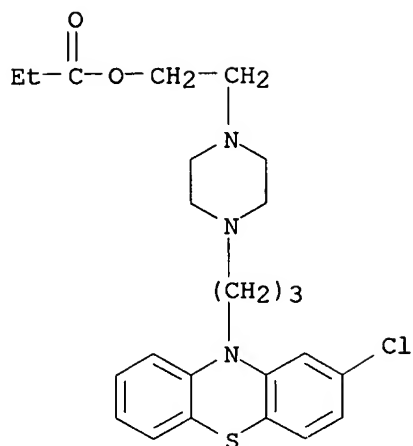
RN 503569-70-8 CAPLUS

CN Benzenebutanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



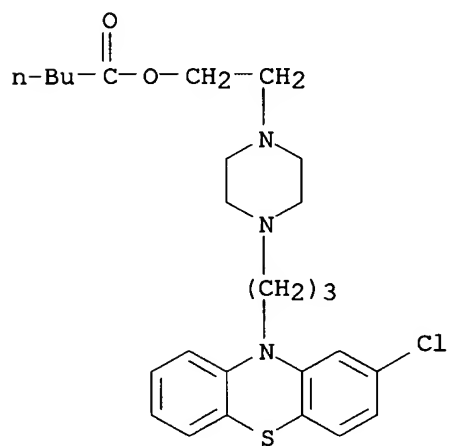
RN 503569-72-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, propanoate (ester) (9CI) (CA INDEX NAME)



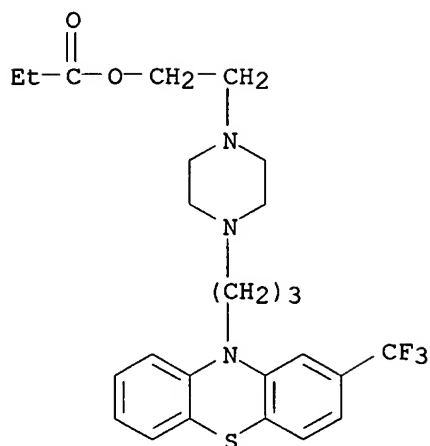
RN 503569-73-1 CAPLUS

CN Pentanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



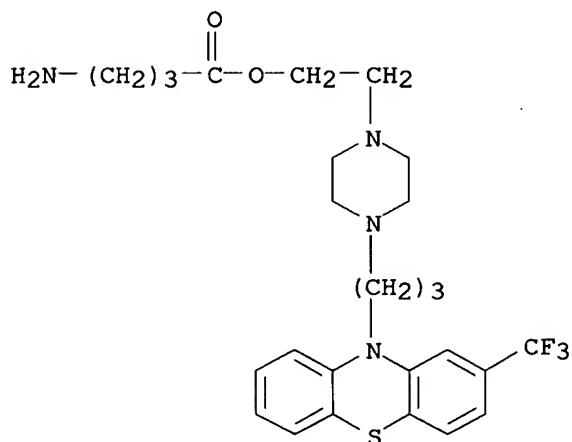
RN 503569-74-2 CAPLUS

CN 1-Piperazineethanol, 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-, propanoate (ester) (9CI) (CA INDEX NAME)



RN 503569-75-3 CAPLUS

CN Butanoic acid, 4-amino-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

IT 84-06-0D, Thiopropazate, organic acid conjugates

RL: PAC (Pharmacological activity); THU (Therapeutic use);

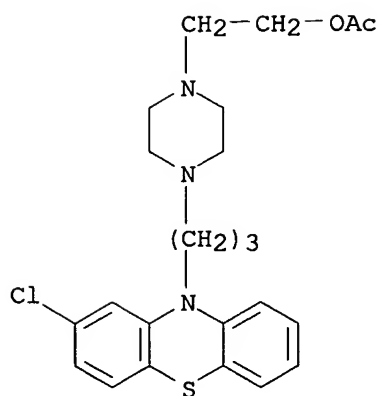
BIOL (Biological study); USES (Uses)

(organic acid-conjugated antipsychotic drugs, and therapeutic use)

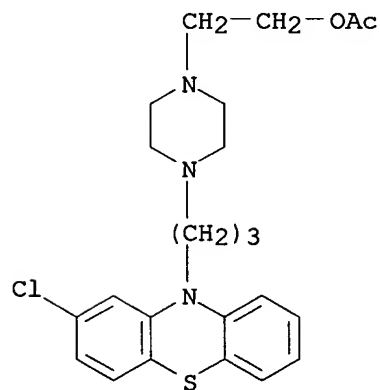
RN 84-06-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)

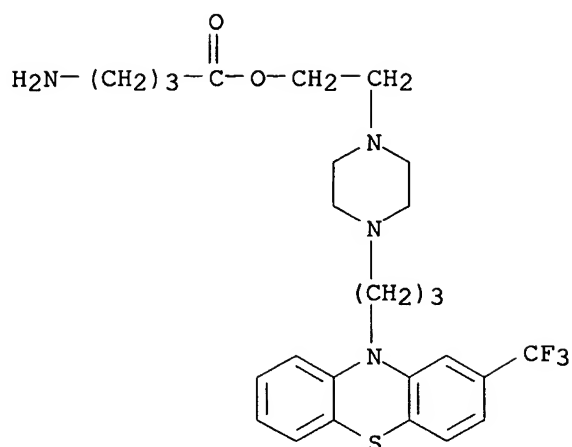




IT 84-06-0, Thiopropazate 503537-31-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (organic acid-conjugated antipsychotic drugs, and therapeutic use)  
 RN 84-06-0 CAPLUS  
 CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-, acetate (ester) (9CI) (CA INDEX NAME)



RN 503537-31-3 CAPLUS  
 CN Butanoic acid, 4-amino-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



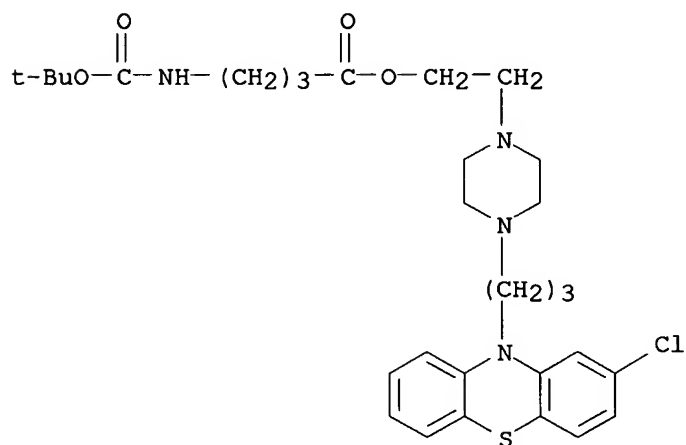
IT 503537-30-2P 503537-32-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(organic acid-conjugated antipsychotic drugs, and therapeutic use)

RN 503537-30-2 CAPLUS

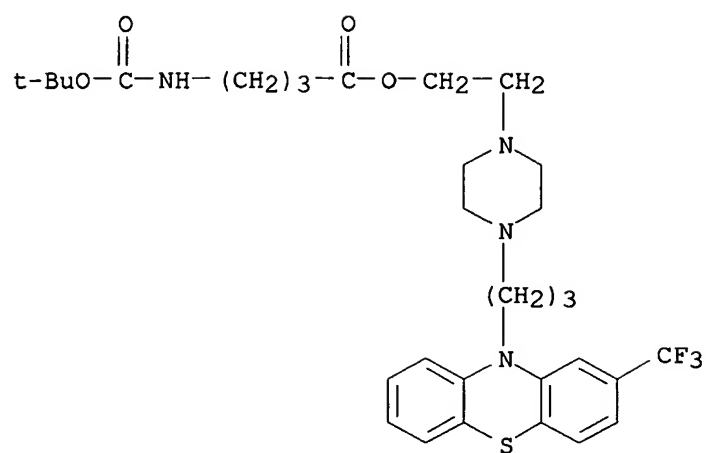
CN Butanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 503537-32-4 CAPLUS

CN Butanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]-, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)

10/808,541



10/808,541

141 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:231020 CAPLUS

DOCUMENT NUMBER: 138:396079

TITLE: Switching from depot antipsychotic drugs to olanzapine in patients with chronic schizophrenia

AUTHOR(S): Godleski, Linda S.; Goldsmith, L. Jane; Vieweg, W. Victor; Zettwoch, Nancy C.; Stikovac, Dejzi M.; Lewis, Susan J.

CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Louisville, KY, USA

SOURCE: Journal of Clinical Psychiatry (2003), 64(2), 119-122  
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Patients with chronic schizophrenia (DSM-IV criteria) often receive depot antipsychotic medications to assure longer administration and better compliance with their treatment regimen. This study evaluated whether patients stabilized on depot antipsychotic medication could be successfully transitioned to oral olanzapine. In a 3-mo open-label study, 26 clin. stable patients with schizophrenia taking depot antipsychotics for over 3 yr were randomly assigned to continue on their current depot dose or to switch to oral olanzapine. Clin. ratings (Pos. and Neg. Syndrome Scale [PANSS], Global Assessment of Functioning [GAF] scale, and Clin. Global Impressions [CGI] scale) and side effect parameters (Abnormal Involuntary Movement Scale [AIMS], Barnes Akathisia Scale, AMDP-5 scale, vital signs, and weight) were obtained monthly. Oral olanzapine patients (N = 13) demonstrated significant clin. improvement over the depot control group (N = 13) from baseline to 3-mo endpoint (PANSS total,  $p = .012$ ; PANSS general,  $p = .068$ ; PANSS neg.,  $p = .098$ ; CGI-Improvement,  $p = .007$ ; CGI-Severity,  $p = .026$ ; GAF,  $p = .015$ ). Side effect rating scales showed no statistical differences between the 2 groups (AIMS, Barnes Akathisia Scale, AMDP-5, vital signs). The depot control group showed no statistical superiority in any measure except weight change ( $p = .0005$ ). After 3 mo, all olanzapine patients preferred olanzapine to their previous depot medications and chose to continue on olanzapine treatment. Clinicians may expect clin. improvement when switching chronically psychotic patients from traditional depot antipsychotic drugs to oral olanzapine. Switching may be completed within a 4-wk period with relative compliance being maintained and patients preferring oral olanzapine to their previous depot medications.

IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); PAC

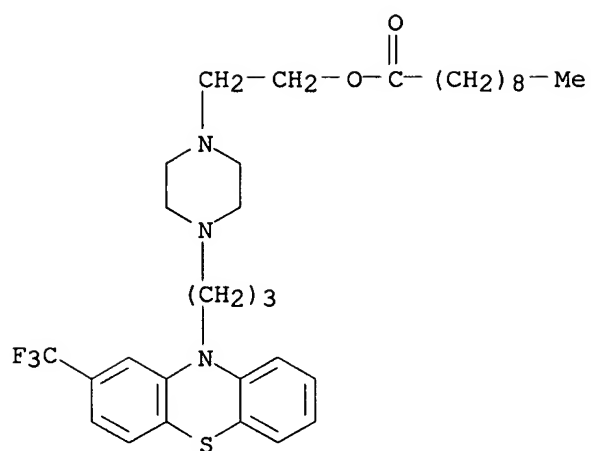
(Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(switching from depot antipsychotic drugs to olanzapine in patients with chronic schizophrenia)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

19

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

E41 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:59291 CAPLUS

DOCUMENT NUMBER: 138:117593

TITLE: The prescription of dexamphetamine to patients with schizophrenia and amphetamine dependence

AUTHOR(S): Carnwath, Tom; Garvey, Tim; Holland, Mark

CORPORATE SOURCE: Substance Misuse Service, Trafford NHS Trust, Sale, Manchester, UK

SOURCE: Journal of Psychopharmacology (London, United Kingdom) (2002), 16(4), 373-377

CODEN: JOPSEQ; ISSN: 0269-8811

PUBLISHER: Sage Publications Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Patients with a severe mental illness such as schizophrenia have significant rates of concurrent amphetamine use. Such dual diagnosis patients have been shown to have poorer treatment outcomes. Often, they do not comply with treatment plans and have frequent episodes of hospitalization. There is growing evidence for the role of prescribed dexamphetamine in the treatment of amphetamine dependence. The prescription of dexamphetamine to patients with schizophrenia and amphetamine dependence has not been previously reported. Eight schizophrenic patients are described to whom dexamphetamine has been prescribed, with information being extracted retrospectively from case notes. In four out of eight cases, the prescription of dexamphetamine led to apparently good progress both in terms of substance misuse and psychiatric health. In two cases, progress was more equivocal, but appeared to produce some benefit. Two cases could be judged as treatment failures, but the condition and situation of the patients were not worse at the end of treatment than at the beginning. Compliance with neuroleptics increased in most cases. No patients exhibited exacerbation of psychosis as a result of treatment. The rate of outcome success is satisfactory when consideration is given to the difficult nature of this patient group, and their previous failure to respond to intensive treatment. It is argued that benefits may be gained from increased compliance with psychiatric treatment in patients prescribed amphetamine, and that this may outweigh possible risks. However, any conclusions are tentative in view of the nature of this study. A small open-label prospective study is recommended.

IT 5002-47-1, Fluphenazine decanoate

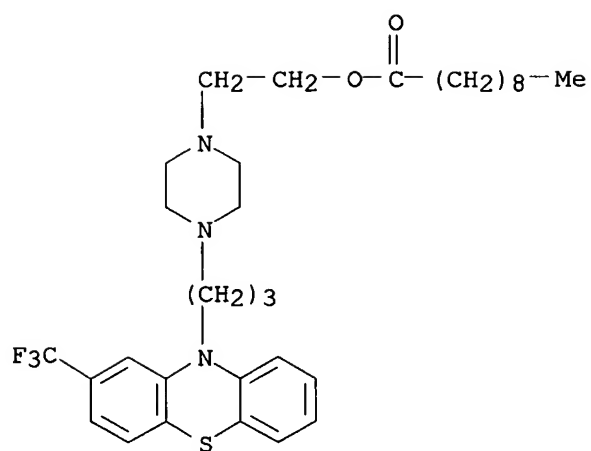
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(prescription of dexamphetamine to patients with schizophrenia and amphetamine dependence)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

25

THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/808,541

L41 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:977588 CAPLUS

DOCUMENT NUMBER: 138:33362

TITLE: Use of cyclooxygenase 2 (COX-2) inhibitors for the treatment of schizophrenia, delusional disorders, affective disorders, autism, or tic disorders

INVENTOR(S): Muller, Norbert

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102297	A2	20021227	WO 2002-EP6013	20020531
WO 2002102297	A3	20030501		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10129320	A1	20030410	DE 2001-10129320	20010619
CA 2448025	AA	20021227	CA 2002-2448025	20020531
EP 1397145	A2	20040317	EP 2002-738138	20020531
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004534066	T2	20041111	JP 2003-504886	20020531
EP 1627639	A2	20060222	EP 2005-24864	20020531
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2004204469	A1	20041014	US 2004-480600	20040205
PRIORITY APPLN. INFO.:			DE 2001-10129320	A 20010619
			US 2002-364904P	P 20020314
			EP 2002-738138	A3 20020531
			WO 2002-EP6013	W 20020531

OTHER SOURCE(S): MARPAT 138:33362

AB The invention discloses the use of a COX-2 inhibitor for the treatment of psychiatric disorders, e.g. schizophrenia, delusional disorders, affective disorders, autism or tic disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders, depressive episodes, recurring depressive episodes, manic episodes and bipolar affective disorders. Moreover, the invention discloses the use of a COX-2 inhibitor, in particular celecoxib, in combination with a neuroleptic drug, in particular risperidone, or an antidepressant, for the treatment of psychiatric disorders such as schizophrenia, delusional disorders, affective disorders, autism or tic disorders.

IT 2746-81-8, Fluphenazine enanthate 5002-47-1, ,  
Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);



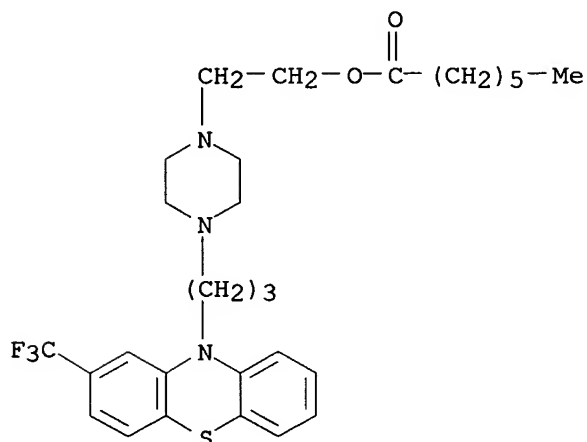
10/808,541

BIOL (Biological study); USES (Uses)

(cyclooxygenase 2 inhibitors for treatment of psychiatric disorders,  
and use with other agents)

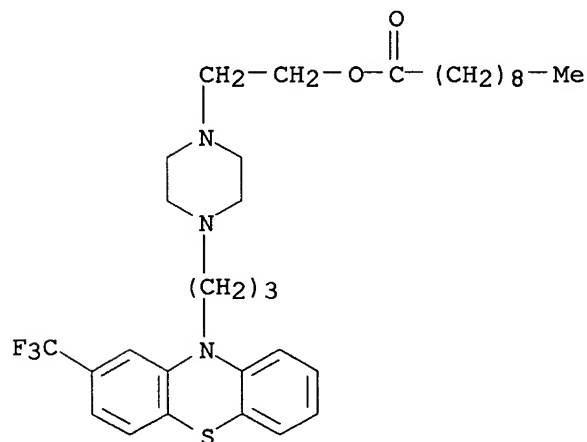
RN 2746-81-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



141 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:797246 CAPLUS

DOCUMENT NUMBER: 139:15

TITLE: Antipsychotics: impact on prolactin levels

AUTHOR(S): Goodnick, Paul J.; Rodriguez, Lucero; Santana, Orlando

CORPORATE SOURCE: Department of Psychiatry & Behavioural Sciences,  
University of Miami School of Medicine, Miami, FL, USA

SOURCE: Expert Opinion on Pharmacotherapy (2002) 3(10),  
1381-1391

CODEN: EOPHF7; ISSN: 1465-6566

PUBLISHER: Ashley Publications Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

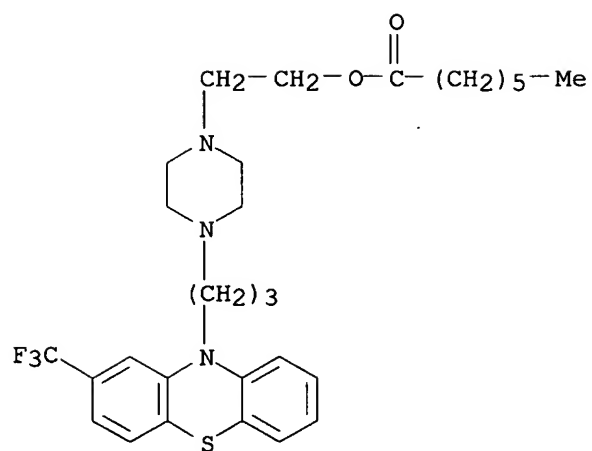
AB A review. Hyperprolactinemia has been associated with a variety of side effects including amenorrhea, galactorrhea, sexual dysfunction, breast engorgement and osteoporosis. Since the mid-1970s, the impact of antipsychotics on human prolactin (hPrl) levels has been investigated. Baseline levels of hPrl were found to be similar in healthy controls and patients who were diagnosed as having schizophrenia. Short-term acute studies done after single parenteral or oral doses of phenothiazines found rapid two- to tenfold increases in hPrl. Similar increases were found in longer term studies that reported increases of three times in both men and women after 3 days that doubled again after several weeks of treatment. A study of longer term injectable fluphenazine enanthate found that elevation induced by a single injection lasted up to 28 days. The same results with significant increases have been reported with the butyrophenone, haloperidol. Substantial increases are found after single injections (up to nine times) and after weeks of treatment (up to three times sustained). Thus, early literature believed that there might be an association between these induced changes and response to therapy. However, prolactin is secreted by the anterior pituitary and is under inhibitory control of dopamine released from the tuberoinfundibular neurons. Thus, increases in prolactin are due to antipsychotic impact on tuberoinfundibular tract, one of four dopamine-related tracts. With the application of clozapine and other atypical antipsychotics, it was found that medications can successfully treat psychosis without increasing hPrl. In fact, early single-dose trials found clozapine to reduce hPrl by 16%. Later studies replicated this result and also found that up to 6 wk of administration led to redns. in hPrl of up to 80%. Risperidone, however, has been found to persistently elevate hPrl in studies, despite its impact on other receptor sites. Olanzapine, quetiapine and ziprasidone have all been found to have little effect or produce decreases in hPrl. Most recently, aripiprazole, in early studies, appears to produce significant redns. in hPrl while maintaining therapeutic efficacy for psychosis.

IT 2746-81-8, Fluphenazine enanthate

RL: ADV (Adverse effect, including toxicity); PAC  
(Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(antipsychotics impact on prolactin levels)

RN 2746-81-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

47

THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:574914 CAPLUS

DOCUMENT NUMBER: 137:119653

TITLE: Combinations of drugs (e.g., chlorpromazine and pentamidine) for the treatment of neoplastic disorders

INVENTOR(S): Borisy, Alexis; Keith, Curtis; Foley, Michael A.; Stockwell, Brent R.

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058684	A2	20020801	WO 2001-US47959	20011030
WO 2002058684	A3	20030417		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6569853	B1	20030527	US 2000-706929	20001106
CA 2436799	AA	20020801	CA 2001-2436799	20011030
EE 200300212	A	20030815	EE 2003-212	20011030
EP 1339399	A2	20030903	EP 2001-994213	20011030
EP 1339399	B1	20060301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015166	A	20031230	BR 2001-15166	20011030
JP 2004517915	T2	20040617	JP 2002-559018	20011030
NZ 525773	A	20050429	NZ 2001-525773	20011030
AT 318590	E	20060315	AT 2001-994213	20011030
US 2003166642	A1	20030904	US 2003-347714	20030121
US 6846816	B2	20050125		
NO 2003002036	A	20030704	NO 2003-2036	20030506
BG 107831	A	20040227	BG 2003-107831	20030520
US 2005192274	A1	20050901	US 2004-24303	20041228
AU 2006200697	A1	20060309	AU 2006-200697	20060220
PRIORITY APPLN. INFO.:				
			US 2000-706929	A1 20001106
			AU 2002-246636	A3 20011030
			WO 2001-US47959	W 20011030
			US 2003-347714	A1 20030121

OTHER SOURCE(S): MARPAT 137:119653

AB The invention features a method for treating a patient having a cancer or other neoplasm, by administering to the patient (i) chlorpromazine or a metabolite or analog thereof; and (ii) pentamidine or a metabolite or analog thereof simultaneously or within 14 days of each other in amts. sufficient to inhibit the growth of the neoplasm.

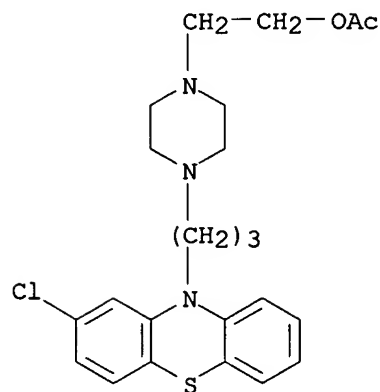
IT 84-06-0, Thiopropazate 17528-28-8, Perphenazine enanthate

10/808,541

RL: PAC (Pharmacological activity); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(drug combinations for treatment of neoplastic disorders)

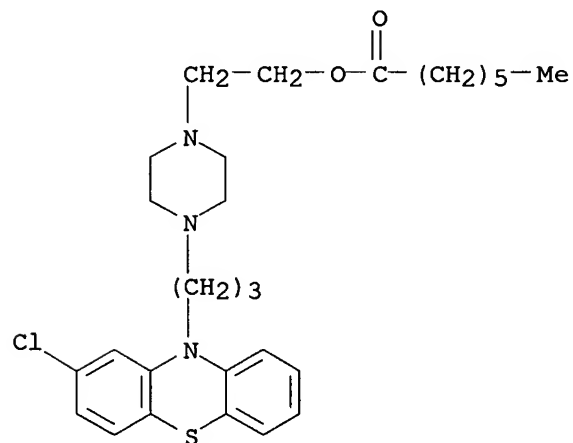
RN 84-06-0 CAPLUS

CN 1-Piperazineethanol, 4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-,  
acetate (ester) (9CI) (CA INDEX NAME)



RN 17528-28-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



10/808,541

L41 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:141165 CAPLUS

DOCUMENT NUMBER: 136:288985

TITLE: Vitamin B6 as add-on treatment in chronic schizophrenic and schizoaffective patients: A double-blind, placebo-controlled study

AUTHOR(S): Lerner, Vladimir; Miodownik, Chanoch; Kaptsan, Alexander; Cohen, Hagit; Loewenthal, Uri; Kotler, Moshe

CORPORATE SOURCE: Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Be'er-Sheva, Israel

SOURCE: Journal of Clinical Psychiatry (2002), 63(1), 54-58  
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vitamin B6, or pyridoxine, plays an intrinsic role in the synthesis of certain neurotransmitters that take part in development of psychotic states. Several reports indicate that vitamin B6 may be a factor in a number of psychiatric disorders and related conditions, such as autism, Alzheimer's disease, hyperactivity, learning disability, anxiety disorder, and depression. Moreover, there are anecdotal reports of a reduction in psychotic symptoms after vitamin B6 supplementation of psychopharmacol. treatment of patients suffering from schizophrenia or organic mental disorder. The aim of this study was to examine whether vitamin B6 therapy influences psychotic symptoms in patients suffering from schizophrenia and schizoaffective disorder. The effects of the supplementation of vitamin B6 to antipsychotic treatment on pos. and neg. symptoms in 15 schizophrenic and schizoaffective patients (DSM-IV criteria) were examined in a double-blind, placebo-controlled, crossover study spanning 9 wk. All patients had stable psychopathol. for at least 1 mo before entry into the study and were maintained on treatment with their prestudy psychoactive and antiparkinsonian medications throughout the study. All patients were assessed using the Pos. and Neg. Syndrome Scale (PANSS) for schizophrenia on a weekly basis. Patients randomly received placebo or vitamin B6, starting at 100 mg/day in the first week and increasing to 400 mg/day in the fourth week by 100-mg increments each week. PANSS scores revealed no differences between vitamin B6- and placebo-treated patients in amelioration of their mental state. Further studies with larger populations and shorter duration of illness are needed to clarify the question of the possible efficacy of vitamin B6 in treatment of psychotic symptoms in schizophrenia.

IT 5002-47-1, Fluphenazine decanoate

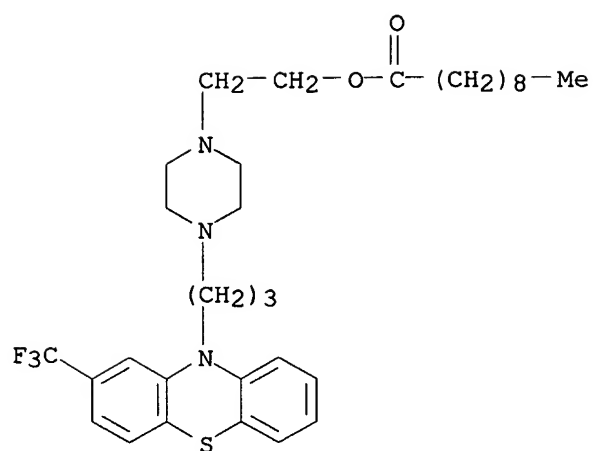
RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(vitamin B6 as add-on treatment in chronic schizophrenic and schizoaffective patients)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

25

THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:663236 CAPLUS

DOCUMENT NUMBER: 136:334764

TITLE: Systemic relaxin in pregnant pony mares grazed on endophyte-infected fescue: effects of fluphenazine treatment

AUTHOR(S): Ryan, P. L.; Bennett-Wimbush, K.; Vaala, W. E.; Bagnell, C. A.

CORPORATE SOURCE: Department of Molecular Biology, Princeton University, Princeton, NJ, USA

SOURCE: Theriogenology (2001), 56(3), 471-483

CODEN: THGNBO; ISSN: 0093-691X

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tall fescue is one of the most widely grown forage grasses for horses in the United States. However, it is frequently infected with the endophyte *Neotyphodium coenophialum* which produces ergot alkaloids that cause severe adverse effects in the pregnant mare. The objectives of this study were to determine the effects of fescue toxicosis and fluphenazine on circulating relaxin in pregnant pony mares and evaluate the usefulness of relaxin as a monitor of treatment efficacy. Twelve mares were maintained on endophyte-infected tall fescue pasture. Group TRT (n = 6), received 25 mg of fluphenazine decanoate (i.m.) on Day 320 of gestation while Group UTRT served as untreated controls. Daily blood samples were collected from Day 300 of gestation until Day 3 post partum and analyzed for plasma relaxin concns. using a homologous equine RIA. Mean gestation lengths were  $330 \pm 0.7$  and  $336.5 \pm 3.2$  days for TRT and UTRT mares, resp. ( $P = 0.07$ ). Mean plasma relaxin concns. in both groups of mares during the week before treatment (Day 313 to 319) were not different (UTRT,  $53.4 \pm 11.3$  ng/mL; TRT,  $61.4 \pm 9.3$  ng/mL). In the week after treatment (Day 320 to 326), mean plasma relaxin tended to be higher ( $P = 0.1$ ) in TRT mares ( $66.7 \pm 6.2$  ng/mL) when compared with UTRT mares ( $49.6 \pm 6.6$  ng/mL), representing a  $17.1$  ng/mL difference in circulating relaxin between the two groups. Systemic relaxin during the last week before delivery (days relative to parturition) for UTRT and TRT mares was  $45.7 \pm 6.7$  and  $64.7 \pm 6.4$  ng/mL ( $P = 0.06$ ), resp. At Day -8 and Day -5 relative to parturition, systemic relaxin in TRT mares was significantly higher ( $P < 0.05$ ) than in UTRT mares. Three of the six UTRT mares and one TRT mare showed clin. symptoms of fescue toxicosis. In the week before delivery, circulating relaxin in mares with problematic pregnancies ( $39.9 \pm 7.8$  ng/mL) was significantly lower than concns. measured in mares with normal pregnancies ( $63.4 \pm 5.4$  ng/mL;  $P = 0.03$ ). Clin. observations suggest that a one-time injection with fluphenazine improved pregnancy outcome by reducing the adverse effects of fescue toxicosis concomitant with a stabilization of plasma relaxin concns. These data support the hypothesis that systemic relaxin may be a useful biochem. means of monitoring placental function and treatment efficacy in the mare.

IT 5002-47-1, Fluphenazine decanoate

RL: PAC (Pharmacological activity); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

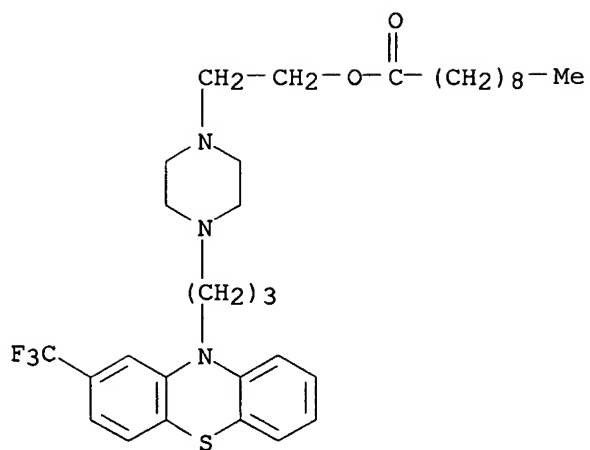
(systemic relaxin in pregnant pony mares grazed on endophyte-infected fescue: fluphenazine treatment)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



10/808,541



REFERENCE COUNT:

45

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:154679 CAPLUS

DOCUMENT NUMBER: 132:274245

TITLE: Neuroleptic-induced striatal damage in rats: a study of antioxidant treatment using accelerometric and immunocytochemical methods

AUTHOR(S): Lohr, James B.; Caligiuri, Michael P.; Manley, Michael S.; Browning, John A.

CORPORATE SOURCE: VA San Diego Healthcare System and Department of Psychiatry, University of California, San Diego, CA, USA

SOURCE: Psychopharmacology (Berlin) (2000), 148(2), 171-179  
CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Investigators have postulated that neuroleptic medications may affect the motor system through the creation of free radicals. Also, structural brain changes related to oxidative damage may disrupt normal striatal function. The goals of this study were to examine whether an antioxidant diet reduced the abnormal movements caused by long-term neuroleptic exposure and to examine structural effects within specific striatal regions in rats. Rats were given a basal diet or a diet high in antioxidants for 4 mo, and treated with 10 mg/kg fluphenazine decanoate or sesame seed oil IM every 2 wk. At baseline and after treatment, head movements were quantified by accelerometry, and immunocytochem. stained cholinergic neurons in the ventrolateral, mediodorsal, and ventromedial regions of the striatum were quantified. Rats treated with fluphenazine had significantly lower neuron densities than those that did not receive antioxidants. Rats exposed to a diet consisting of antioxidants had significantly higher neuron densities than those that did not receive antioxidants in each of the three regions tested. Rats treated with fluphenazine had a greater increase in the number of accelerometric peaks recorded per min compared with untreated animals. The increase in the number of accelerometric peaks recorded per min was lower for animals exposed to antioxidant diets compared with unexposed animals. Lastly, there was a significant correlation between the accelerometric peak change score and cholinergic neuron d. in all three regions. Thus, long-term neuroleptic treatment is associated with an increase in head movements and a reduction in ChAT-stained striatal cholinergic neurons and that these abnormalities are reduced by antioxidants.

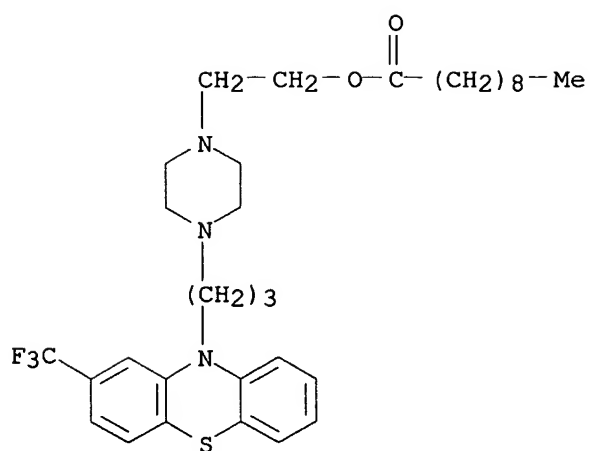
IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)

(neuroleptic-induced striatal damage in rats: effects of antioxidant diet)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

55

THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:640966 CAPLUS

DOCUMENT NUMBER: 131:241994

TITLE: Use of stimulated peripheral blood mononuclear cells for the treatment of brain-related diseases, disorders and damage

INVENTOR(S): Wank, Rudolf

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950393	A2	19991007	WO 1999-EP2225	19990331
WO 9950393	A3	19991118		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9933330	A1	19991018	AU 1999-33330	19990331
EP 1068299	A2	20010117	EP 1999-914560	19990331
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002509942	T2	20020402	JP 2000-541281	19990331
PRIORITY APPLN. INFO.:			DE 1998-19814701	A 19980401
			WO 1999-EP2225	W 19990331

AB The invention relates to the use of stimulated peripheral blood mononuclear cells (PBMC) for the treatment of brain-related diseases, disorders and damage, such as manic-depressive illness or manic-depressive psychosis, schizophrenia, depressive syndromes without endogenous cause, autism, disturbances of cerebral development during and after the embryonal stage, Downs syndrome, brain damage due to accidents or other causes, and Parkinson's disease. After activation of the PBMC the stimulated cells can possibly also be treated with gamma-interferon and/or alpha-interferon.

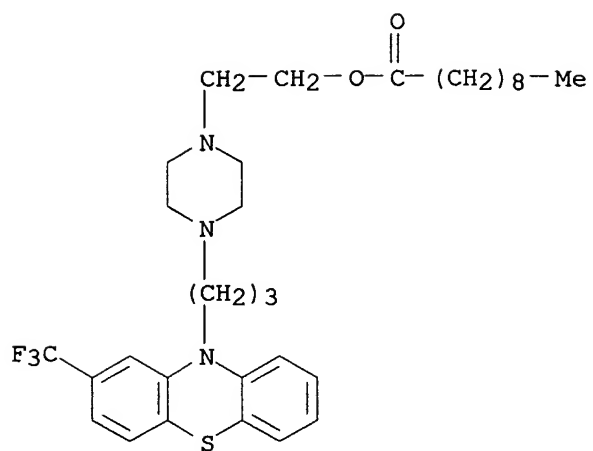
IT 5002-47-1, Fluphenazine decanoate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of stimulated peripheral blood mononuclear cells and antibiotics for treatment of brain-related diseases, disorders and damage)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:649470 CAPLUS

DOCUMENT NUMBER: 130:50798

TITLE: Tardive dyskinesia and serum iron indices

AUTHOR(S): Wirshing, Donna A.; Bartzokis, George; Pierre, Joseph M.; Wirshing, William C.; Sun, Albert; Tishler, Todd A.; Marder, Stephen R.

CORPORATE SOURCE: The Psychiatry Service, West Los Angeles VA Medical Center, Los Angeles, CA, USA

SOURCE: Biological Psychiatry (1998), 44(6), 493-498

CODEN: BIPCBF; ISSN: 0006-3223

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study was undertaken to evaluate whether peripheral (serum) markers of iron status are associated with severity of the choreoathetoid movements seen in tardive dyskinesia (TD). Serum iron indexes (ferritin, iron, and total iron binding capacity) and fluphenazine levels were measured in a group of 30 male DSM-III diagnosed schizophrenic patients chronically treated with fluphenazine decanoate. The severity of choreoathetoid movements was assessed with the Abnormal Involuntary Movement Scale (AIMS), and akathisia was assessed with the Barnes scale. A significant pos. correlation was observed between AIMS scores and serum ferritin. This relationship remained significant after controlling for age and plasma fluphenazine levels. No significant correlations were observed between serum iron or total iron binding capacity and choreoathetoid movement ratings. There were no significant assocns. between serum iron indexes and akathisia ratings. The data suggest that choreoathetoid movements are associated with serum ferritin levels in chronically medicated male schizophrenic patients. This relationship does not seem to be caused by an association of these variable with age or plasma fluphenazine levels. In addition, the relationship seems to be specific, since other iron indexes and another extrapyramidal side effect (akathisia) do not demonstrate a similar relationship. In view of reports that antipsychotic medications change normal iron metabolism and increase iron uptake into the brain, the current results could be interpreted to suggest that serum ferritin levels may be a risk factor for TD in patients treated with "classic" antipsychotic medications.

IT 5002-47-1, Fluphenazine decanoate

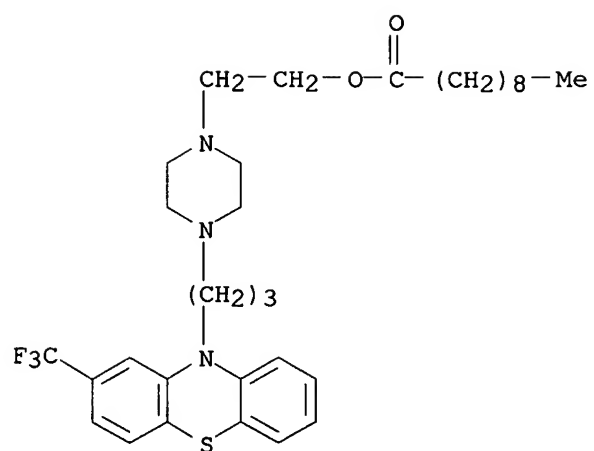
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(tardive dyskinesia and serum iron indexes in human male schizophrenic taking neuroleptic medication)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

48

THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:306797 CAPLUS

DOCUMENT NUMBER: 129:76373

TITLE: Increased sister chromatid exchange and chromosomal aberration frequencies in psychiatric patients receiving psychopharmacological therapy

AUTHOR(S): Bigatti, M. Paola; Corona, Daniela; Munizza, Carmine

CORPORATE SOURCE: Dipartimento di Biologia Animale e dell'Uomo, Universita di Torino, Turin, Italy

SOURCE: Mutation Research (1998), 413(2), 169-175

CODEN: MUREAV; ISSN: 0027-5107

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Combinations of various psychotropic drugs are often used, sometimes for long periods, in the treatment of various forms of psychiatric disorders. This paper evaluates the cytogenetic consequences of daily exposure to polytherapy with antianxiety, antipsychotic and antimanic drugs by determining chromosomal aberrations (CA) and sister chromatid exchange (SCE) in peripheral blood samples. The study was performed with a group of 36 psychiatric patients: 18 receiving long-term treatment with lithium carbonate, combined with benzodiazepines (BD) and antipsychotic agents (Group A) and 18 treated with BD and antipsychotics (Group B). Among the latter, 7 patients had only been treated for 1 mo (Group B1). The results reveal a significant increase ( $p < 0.01$ ) in cells with aberrations in the two groups of patients (A, B) compared to controls. Moreover, complex aberrations (dicentrics, rearrangements, chromatid exchanges) had a frequency of 0.63% in patients receiving long-term treatment compared to 0.11% in controls, corresponding to the general spontaneous rate. The mean frequency of SCE/cell and the percentage of cells with a high frequency of exchanges (HFC) also showed a highly significant difference compared to controls in both Group A and Group B. Group B1 (patients who only commenced treatment 1 mo earlier) did not differ from the control group with regard to the frequency and type of chromosomal aberration or in relation to the mean frequency of SCE/cell. No significant differences were detected between Groups A and B both of which showed similar frequencies of cells with aberrations, SCE/cell and HFC. No correlations were observed in Group A between lithemia and the biol. markers studied.

IT 5002-47-1, Fluphenazine decanoate

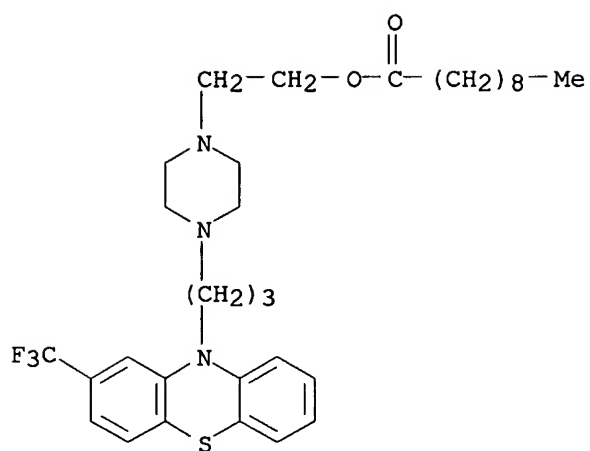
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(genotoxicity in psychiatric patients receiving combined psychopharmacol. therapy)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT:

32

THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:702593 CAPLUS

DOCUMENT NUMBER: 128:45303

TITLE: Photosensitization and photoprotection by some drugs, metabolites and other compounds

AUTHOR(S): Lozovskaya, E. L.; Makareeva, E. N.; Makedonov, Yu. V.; Sapezhinsky, I. I.

CORPORATE SOURCE: Institute of Biochemical Physics, Russian Acad. Sci., Moscow, Russia

SOURCE: Biofizika (1997), 42(3), 549-557

CODEN: BIOFAI; ISSN: 0006-3029

PUBLISHER: Nauka

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Photosensitizing and photoprotecting efficiency of about a hundred compds., mainly drugs, was studied. A method based on chemiluminescence along with photooxidn. of glycytryptophan under irradiation in UVB range in solution was used for testing. As a measure of photosensitizing efficiency, the concentration of photosensitizer which induced two-fold increase of chemiluminescence intensity was chosen. The most effective photosensitizers are riboflavin, FAD, furagin, psoralen, vikasol, benzobarbital, mydocalm, angelicyn, furadonin, ethacridine, diazolin, folic acid. With regard to pharmacol. doses of drugs, more dangerous sensitizers (in descending order) are p-aminosalicylic acid, furagin, riboflavin, benzobarbital, thiopental, chloramphenicol, nicodin, mydocalm, furadonin, oxolonic acid, furazolidone, psoralen, nicotinamide, and diazolin. The photoprotecting effect was determined by the concentration at which

chemiluminescence intensity decreased twice. The most effective photoprotectors were etamsilat, quercetin, ftivazide, chlorpromazine, diprazine, thioridazine, aminophenazone, and oxaphenamide. Concentration dependence for some of these drugs (etamsilat, chlorpromazine, diprazine, thioridazine) is non-monotonous: they inhibited photooxidn. in low

concentration

(about 10<sup>-7</sup>-10<sup>-6</sup> M), but at higher concns. (10<sup>-5</sup>-10<sup>-4</sup> M)

photosensitization dominated over photoprotection.

IT 522-23-6, Frenolon

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(photosensitization and photoprotection by drugs, metabolites, and other compds.)

RN 522-23-6 CAPLUS

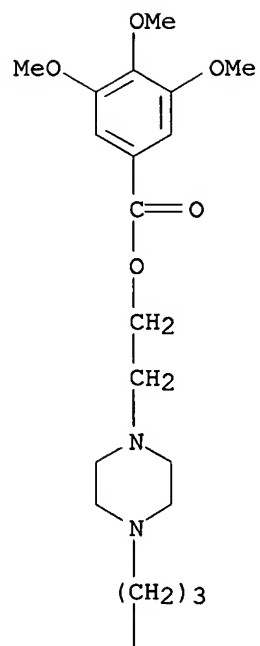
CN Benzoic acid, 3,4,5-trimethoxy-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

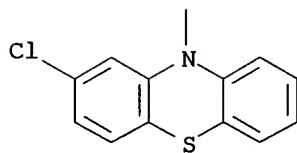
CRN 388-51-2

CMF C31 H36 Cl N3 O5 S

PAGE 1-A



PAGE 2-A

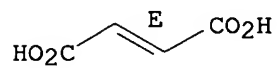


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



L41 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:362762 CAPLUS

DOCUMENT NUMBER: 127:90381

TITLE: Non-functional CYP2D6 alleles and risk for neuroleptic-induced movement disorders in schizophrenic patients

AUTHOR(S): Andreassen, Ole A.; MacEwan, Tom; Gulbrandsen, Anne-Karin; McCreadie, Robin G.; Steen, Vidar M.

CORPORATE SOURCE: Dr. Einar Martens' Res. Group for Biol. Psychiatry, Cent. for Mol. Med., Haukeland Univ. Hosp., Bergen, N-5021, Norway

SOURCE: Psychopharmacology (Berlin) (1997), 131(2), 174-179  
CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The use of classic antipsychotic drugs in the long-term treatment of schizophrenia is associated with risk for extrapyramidal side-effects, such as akathisia, parkinsonism and tardive dyskinesia (TD). Approx. 5-10% of European Caucasians lack the cytochrome P 450 enzyme CYP2D6 (so-called poor metabolizers; PM), which normally metabolizes several drugs including many neuroleptics. PM subjects may achieve high or toxic plasma levels upon standard drug therapy. In this study we have examined 100 subjects from the Nithsdale cohort of schizophrenic patients in South-west Scotland receiving long-term neuroleptic medication, which enabled us to perform both a cross-sectional and longitudinal evaluation of extrapyramidal side-effects in relation to the genetically impaired CYP2D6 metabolism. We identified ten (10%) schizophrenic subjects with the PM genotype. In the cross-sectional study, the prevalence of TD, parkinsonism and akathisia was 51%, 38% and 15%, resp. Patients with TD or parkinsonism were significantly older than patients without these side-effects. In contrast, patients with akathisia were significantly younger than patients without akathisia. There was a non-significant tendency for PM subjects to have more severe ratings for TD and parkinsonism. In the long-term evaluation based on repeated ratings since 1981, there was a non-significant 3-fold higher frequency of PM subjects among schizophrenic patients with longitudinal TD, as compared with the groups of patients with fluctuating or no TD. These results indicate that genetically impaired CYP2D6 metabolism may be a contributing factor for the development of persistent TD.

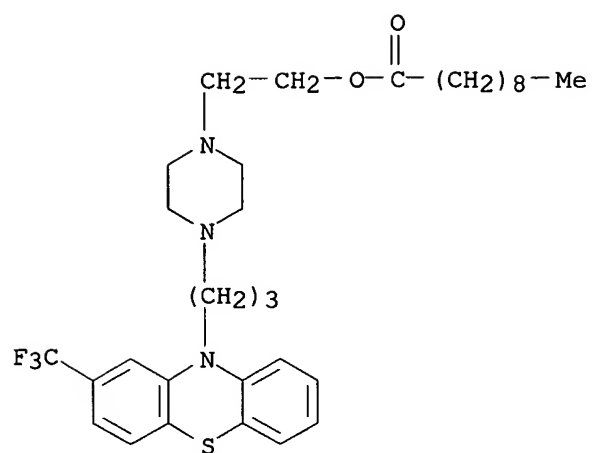
IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(role of non-functional CYP2D6 in neuroleptic-induced movement disorders in schizophrenic patients)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

44

THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:695139 CAPLUS

DOCUMENT NUMBER: 126:42541

TITLE: Effects of subthalamic nucleus lesions in a putative model of tardive dyskinesia in the rat

AUTHOR(S): Stoessl, A. Jon; Rajakumar, Nagalingham

CORPORATE SOURCE: Clinical Neurological Sciences, University Western Ontario, London, ON, N6A 5A5, Can.

SOURCE: Synapse (New York) (1996), 24(3), 256-261

CODEN: SYNAET; ISSN: 0887-4476

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of bilateral excitotoxic lesions of the subthalamic nucleus on vacuous chewing movements induced by chronic neuroleptic therapy were examined in the rat. Fluphenazine decanoate (25 mg/kg i.m. q 3 wk + 24 wk) induced vacuous chewing movements, as previously described. This response was suppressed to control levels in animals tested 1-3 wk following bilateral infusion of quinolinic acid (100 nmol/1 µL per side) into the subthalamic nucleus. Subthalamic nucleus lesions resulted in increased locomotion and sniffing in neuroleptic-naive animals, but these responses were suppressed by concomitant neuroleptic treatment. As vacuous chewing movements induced by chronic neuroleptics are considered to be analogous to tardive dyskinesia in humans, our findings lend further support to the importance of the subthalamic nucleus in the regulation of orofacial movements and suggest that tardive dyskinesia may, in part, be related to altered activity in this structure. This, in turn, suggests that current models of basal ganglia function are inadequate to account for certain pathol. states and require re-examination

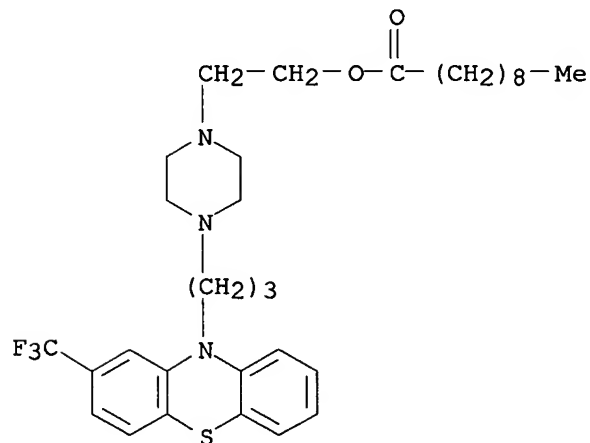
IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(effects of subthalamic nucleus lesions in a putative model of tardive dyskinesia in the rat)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:690802 CAPLUS

DOCUMENT NUMBER: 123:102644

TITLE: Lack of a strong influence of neuroleptic decanoates on dopaminergic and GABAergic functions

AUTHOR(S): Ossowska, Krystyna; Wolfarth, Stanislaw

CORPORATE SOURCE: Institute Pharmacology, Polish Academy Sciences, Krakow, 31-343, Pol.

SOURCE: Polish Journal of Pharmacology (1995), 47(2), 99-107  
CODEN: PJPAE3; ISSN: 1230-6002

PUBLISHER: Polish Academy of Sciences, Institute of Pharmacology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Data concerning the incidence of extrapyramidal symptoms and the development of the supersensitivity to dopamine after administration of depot neuroleptics are controversial. The aim of the study was to examine the influence of depot neuroleptics on the sensitivity of dopamine receptors and GABA nigral receptors. Haloperidol decanoate (30 or 60 mg/kg i.m.) and fluphenazine decanoate (12.5 or 25 mg/kg i.m.) were injected twice at a 15 day interval. These treatments induced weak but very long-lasting catalepsy (60-105 days depending on the neuroleptic and its dose). The only significant enhancement of the apomorphine (0.25 mg/kg s.c.) stereotypy was observed 135 days after the lower dose of haloperidol and 230 days after the lower dose of fluphenazine. Haloperidol decanoate (30 mg/kg) did not influence the number of contralateral rotations induced by muscimol (10 or 25 ng/0.5 µl) injected into the substantia nigra pars reticulata 35, 55 and 135 days after the first injection. Present results indicate that the dopaminergic supersensitivity after administration of depot neuroleptics is weak and appears very late, and that haloperidol decanoate does not induce nigral supersensitivity to GABA. It is suggested that the depot neuroleptics might induce less extrapyramidal symptoms in the clinic than the daily neuroleptic treatment.

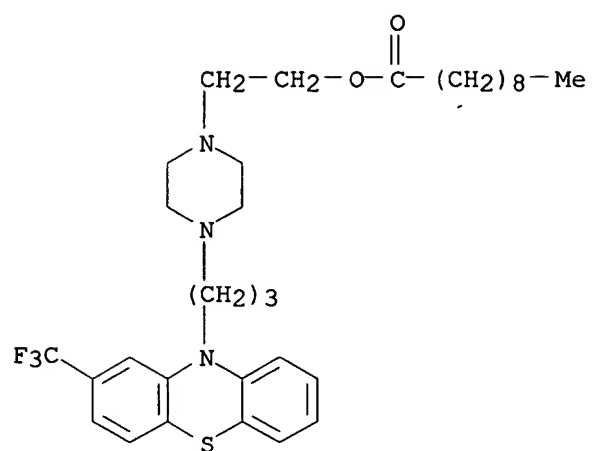
IT 5002-47-1, Fluphenazine decanoate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)

(lack of a strong influence of neuroleptic decanoates on dopaminergic and GABAergic functions)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)





L41 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:509 CAPLUS

DOCUMENT NUMBER: 114:509

TITLE: Mutagenicity test on fluphenazine decanoate

AUTHOR(S): Suzuki, Shuzou; Atai, Hiroshi; Hatakeyama, Yoshiro

CORPORATE SOURCE: Preclin. Res. Lab., Cent. Inst. Exp. Anim., Kawasaki, 213, Japan

SOURCE: Jitchuken Zenrinsho Kenkyuho (1990), 16(1), 71-95

CODEN: JZKEDZ; ISSN: 0385-8502

DOCUMENT TYPE: Journal

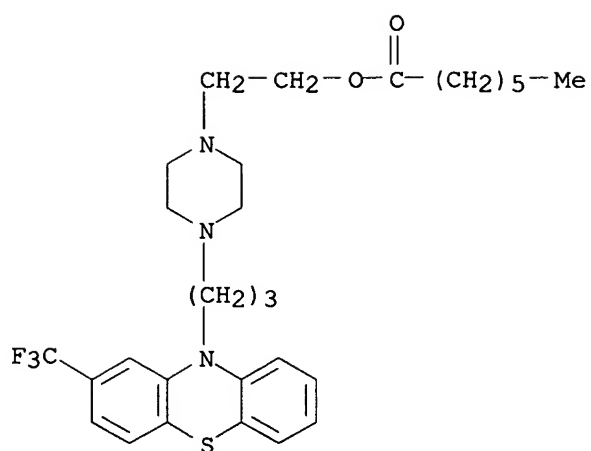
LANGUAGE: Japanese

AB The mutagenicity of fluphenazine decanoate (FD) and its analogs fluphenazine enanthate (FE) and fluphenazine dihydrochloride (FH) were evaluated in a reverse mutation test with bacteria, a chromosomal aberration test with mammalian cells in culture, and a micronucleus test with mice. In the reverse mutation test, each form showed toxicity to bacterial strains, and the order of relative toxic strength was FH > FE > FD. The toxicity of FE was stronger with S9 mix than without, but this tendency was not clear with FD. Each form showed clear-cut toxicity for each bacterial strain, but revertant colonies showed no increase with FD, FE, or FH. Therefore, the result of the reverse mutation test was neg. In the chromosomal aberration test, each form showed clear-cut inhibition of cellular proliferation, and for both the direct and metabolic activation method, this inhibition appeared in the order of intensity of FH > FE > FD. With the metabolic activation method, both FD and FE showed stronger inhibition with S9 mix than without S9 mix. Each form showed toxicity towards the Chinese hamster lung (CHL) cell line, but structural and numerical aberrations of the chromosomes of the CHL cells were not induced by FD, FE, or FH. Therefore, the result of the chromosomal aberration test was neg. In the micronucleus test, no differences in the number and frequency of micronucleated polychromatic erythrocytes were recognized between the FD, FE, and FH groups and the neg. control group. The results seem to indicate that the chromosomal aberration in vivo was not induced by these fluphenazines. Thus, the result of the micronucleus test was neg. These results suggest that fluphenazine has no mutagenicity.

IT 2746-81-8, Fluphenazine enanthate 5002-47-1,  
Fluphenazine decanoate  
RL: ADV (Adverse effect, including toxicity); BIOL  
(Biological study)  
(mutagenicity of, lack of)

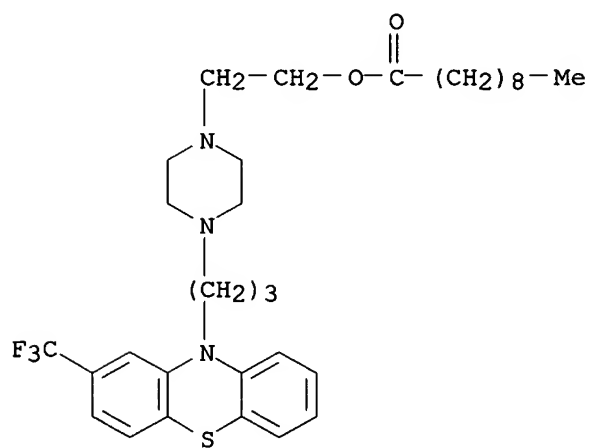
RN 2746-81-8 CAPLUS

CN Heptanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:211321 CAPLUS

DOCUMENT NUMBER: 98:211321

TITLE: Enhancement by fluphenazine of  
dimethylbenz[a]anthracene-induced mammary  
tumorigenesis in rats

AUTHOR(S): Shoyab, Mohammed

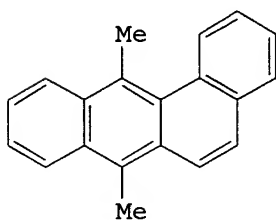
CORPORATE SOURCE: Lab. Viral Carcinogen., Natl. Cancer Inst., Frederick,  
MD, 21702, USASOURCE: Cancer Letters (Shannon, Ireland) (1983), 18(3),  
297-303

CODEN: CALEDQ; ISSN: 0304-3835

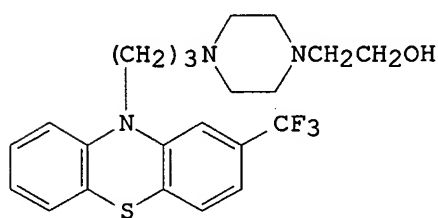
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



II

AB Mammary tumor formation in female rats was studied as a 2-stage protocol of initiation with DMBA (I) [57-97-6] followed by repeated treatment with fluphenazine decanoate (II decanoate) [5002-47-1]. No mammary tumors were found in the untreated control group or in the II-treated groups. The repeated II treatment increased the number of mammary tumors in rats who had previously received DMBA and also shortened the tumor latency period. Thus, some caution should be exercised in prescribing I neuroleptics to individuals at high risk for breast cancer.

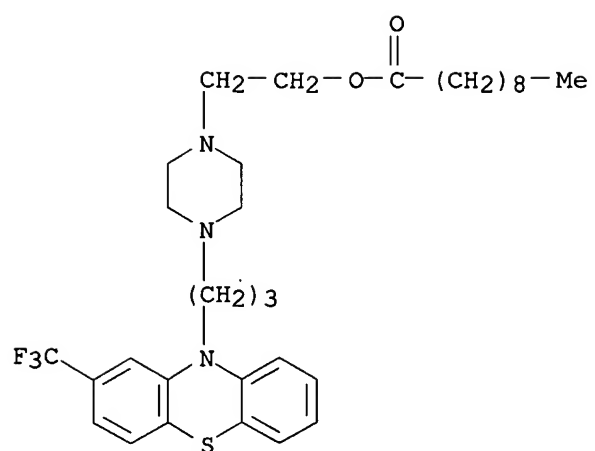
IT 5002-47-1

RL: BIOL (Biological study)

(DMBA-induced mammary tumor enhancement by)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:525903 CAPLUS

DOCUMENT NUMBER: 95:125903

TITLE: Mutagenicity effect of twenty-two psychotropic drugs with the Ames method

AUTHOR(S): Jiang, San-Duo; Lin, Chih-Kuang; Li, Chang-Fu; Jen, Ta-Ming

CORPORATE SOURCE: Shanghai Psychiatric Hygiene, Shanghai, Peop. Rep. China

SOURCE: Ziran Zazhi (1981), 4(6), 478-9

CODEN: TJTCD4; ISSN: 0253-9608

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

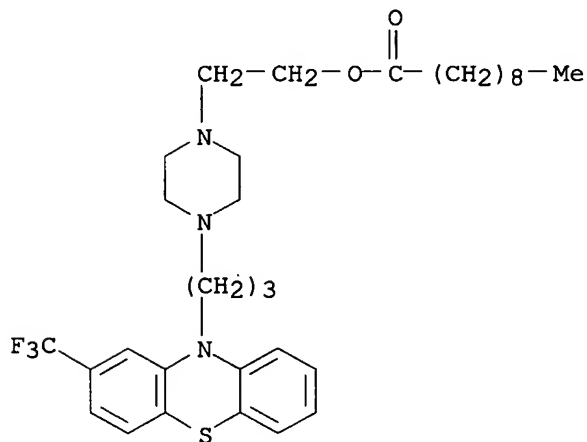
AB Of 22 psychotropic drugs tests, according to the method of N. B. Ames, et al. (1975), only chloral hydrate [302-17-0] showed a noticeable mutagenic effect on amino acid-deficient mutants of *Salmonella typhimurium*. Thus, it is relatively safe to use these psychotropic drugs in clin. practice with the exception of chloral hydrate.

IT 5002-47-1

RL: BIOL (Biological study)  
(mutagenicity in relation to)

RN 5002-47-1 CAPLUS

CN Decanoic acid, 2-[4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-piperazinyl]ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1975:557949 CAPLUS

DOCUMENT NUMBER: 83:157949

TITLE: Action of phenothiazine derivative methophenazine on prenatal development in rats

AUTHOR(S): Horvath, Cecilia; Druga, Alice

CORPORATE SOURCE: Med. Sch., Semmelweis Univ., Budapest, Hung.

SOURCE: Teratology (1975), 11(3), 325-29

CODEN: TJADAB; ISSN: 0040-3709

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Single doses of 100-400 mg/kg or multiple doses of 10 or 50 mg/kg of the phenothiazine derivative methophenazine difumarate (I) [522-23-6] were given per os to rats at various times on the 7th-14th days of gestation and the fetuses examined near term. Results indicated that I was mainly embryo-lethal when administered on the 8th-11th days, and was teratogenic at later times, producing types of malformations that depended on the day of treatment, the most susceptible period being the 13th and 14th days of gestation. Teratogenicity occurred only when the dosages were highly toxic to the pregnant rats. Riboflavin [83-88-5] given ip on the 14th day significantly reduced the embryo-lethal but not the teratogenic action of I.

IT 522-23-6

RL: ADV (Adverse effect, including toxicity); BIOL  
(Biological study)

(teratogenesis from and toxicity of, riboflavin in relation to)

RN 522-23-6 CAPLUS

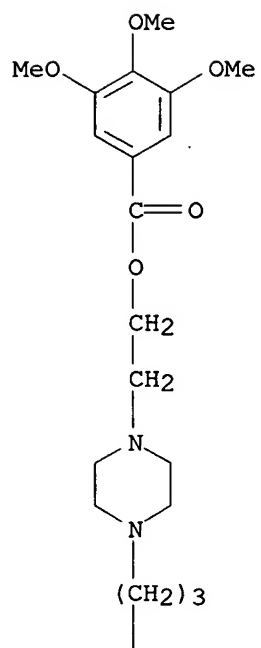
CN Benzoic acid, 3,4,5-trimethoxy-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

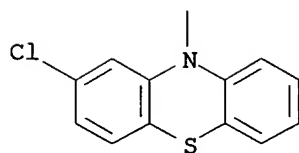
CRN 388-51-2

CMF C31 H36 Cl N3 O5 S

PAGE 1-A



PAGE 2-A

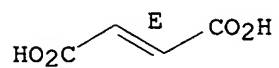


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



L41 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1972:483593 CAPLUS

DOCUMENT NUMBER: 77:83593

TITLE: Experimental-morphological study of the chronic action of phrenolon

AUTHOR(S): Kondrashkova, O. V.; Sokolova, A. P.; Gorbatenko, S. A.

CORPORATE SOURCE: Moscow, USSR

SOURCE: Trudy Moskovskogo Nauchno-Issledovatel'skogo Instituta Psikhiatrii (1970), 61, 196-203

CODEN: TMIPB7; ISSN: 0371-9677

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Daily s.c. injections of 0.3 mg phrenolon (I) [522-23-6]/kg into rats for 2 weeks caused swelling and hyperchromatosis of neurons, proliferation of macroglia and oligodendroglia, and swelling of kidney and liver parenchymata. However, after treatment for 6 weeks, these effects were no longer significant.

IT 522-23-6

RL: ADV (Adverse effect, including toxicity); BIOL  
(Biological study)  
(toxicity of)

RN 522-23-6 CAPLUS

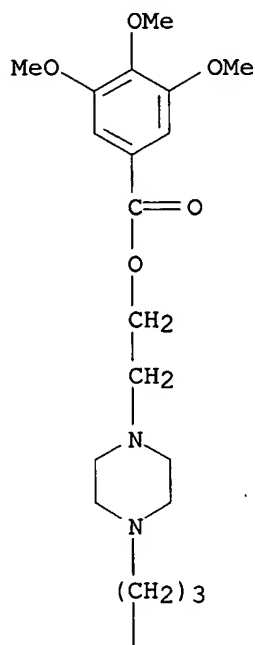
CN Benzoic acid, 3,4,5-trimethoxy-, 2-[4-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-1-piperazinyl]ethyl ester, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

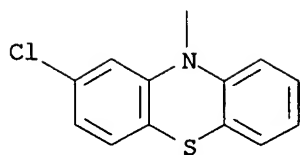
CRN 388-51-2

CMF C31 H36 Cl N3 O5 S

PAGE 1-A





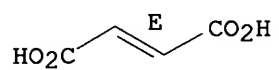


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



10/808,541

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L1 STR  
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ACTIVATE B10808541/A \

L2 STR  
L3 ( 3474)SEA FILE=REGISTRY SSS FUL L2  
L4 STR  
L5 498 SEA FILE=REGISTRY SUB=L3 SSS FUL L4  
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L6 STRUCTURE UPLOADED  
L7 375 S L6 SUB=L5 FUL  
L8 123 S L5 NOT L7

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L9 650 S L7  
L10 ANALYZE L9 1- RN HIT : 238 TERMS

FILE 'REGISTRY' ENTERED AT 09:51:45 ON 12 JUL 2006  
L11 6 S 5002-47-1/RN OR 84-06-0/RN OR 2746-81-8/RN OR 388-51-2/RN OR  
L12 STRUCTURE UPLOADED  
L13 10 S L12 SUB=L5 FUL

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L14 5 S L13

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L15 1 S US20040242570/PN  
SELECT RN L15 1-

FILE 'REGISTRY' ENTERED AT 09:55:19 ON 12 JUL 2006  
L16 69 S E1-69  
L17 18 S 6-6-6/SZ AND L16  
L18 51 S L16 NOT L17  
L19 11 S L18 AND NRS=1  
L20 24 S L18 AND NRS>1  
L21 16 S L18 NOT (L19 OR L20)

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FILE 'REGISTRY' ENTERED AT 10:03:43 ON 12 JUL 2006  
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L23 15730 S L22

FILE 'REGISTRY' ENTERED AT 10:05:04 ON 12 JUL 2006  
L24 1 S PIPERAZINE/CN  
L25 691215 S 46.383.1/RID  
L26 15 S L17 AND L25  
L27 1 S L17 NOT L22  
L28 34120 S C4NS-C6-C6/EA

10/808,541

L29 14 S L26 AND L28

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L30 3111 S L29  
L31 ANALYZE L30 1- RN HIT : 14 TERMS

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L32 3 S 69-23-8/RN OR 58-39-9/RN OR 84-06-0/RN  
L33 11 S L29 NOT L32

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L34 1 S L33  
L35 1 S L32 AND L34  
L36 5 S L14 OR L35  
L37 21 S L9 AND ADV/RL  
L38 29 S L9 AND PAC/RL  
L39 339 S L9 AND BIOL/RL  
L40 42 S L37 OR L38  
L41 42 S L39 AND L40  
L42 46 S L36 OR L41  
L43 604 S L9 NOT L42

=> save l43

ENTER NAME OR (END):d10808541/a

ANSWER SET L43 HAS BEEN SAVED AS 'D10808541/A'

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